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# DERMATOPHYTOSIS AND DERMATOPHYTIDS

## WITH PARTICULAR REFERENCE TO THE DIFFERENTIAL DIAGNOSIS OF DYSHIDROSIFORM ERUPTIONS OF THE HANDS AND FEET

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Interest in the broad subject embraced by the term dyshidrosiform eruptions of the hands and feet has in recent years acquired a tremendous impetus as a result of the discovery that a primary fungous infection of the skin of the feet may give rise to secondary vesicular and other inflammatory lesions on the hands and on other parts of the body.[1]

The incidence of superficial mycotic lesions of the skin has become so widespread in most parts of the world, and especially in this country, that opportunities for study and investigation are unlimited; advantage has been taken of these opportunities by scores of clinical observers and laboratory investigators, with the result that more light is constantly thrown on the various phases and problems connected with dyshidrosiform dermatoses as a whole. These investigations have led to ramifications embracing the fields of atopy, allergy, immunology, mycology, biologic chemistry, serology, pharmacology and chemistry.

With this in mind, we deemed it expedient to restrict ourselves in this address to certain narrower phases of the subject and decided to deal with certain aspects pertaining particularly to the differential diagnosis of a group of dyshidrosiform dermatoses.

Included in this group are the following:

1. Eruptions due to superficial mycotic infections—infections with Trichophyton, Epidermophyton and yeasts.

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The publication of this article was delayed for many months by a discussion of the nomenclature of fungous diseases in general, which the ARCHIVES was trying to unravel.

1. Williams, C. M.: Enlarging Conception of Dermatophytosis, Arch. Dermat. & Syph. **15**:451 (April) 1927.

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2. Eruptions of secondary nature resulting from primary fungous foci—epidermophytids, moniliids and trichophytids.

3. Eruptions caused by exogenous irritants. These fall in the category of dermatitis venenata, occupational dermatoses, trade eczemas, industrial dermatoses, dermatitis eczematosa and so forth. These eruptions are encountered most frequently among dyers, furriers, painters, tanners, leather-workers, barbers, hair-dressers, photographers, workers in ammunition and rubber factories, and in the electrical and oil industries, printers, typesetters, persons who handle food, florists, chemists, druggists, surgeons, dentists, nurses and persons in scores of other occupations and professions.

4. Vesicular eruptions of unknown cause—"eczema," dermatitis eczematosa and pompholyx.

5. Toxic eruptions caused by drugs, foods, etc.

The fact is known to all dermatologists that the dyshidrosiform eruptions representing these five groups are, with certain exceptions, clinically indistinguishable from one another in a large proportion of unselected patients. We stress the term unselected patients, because this statement evidently would not be applicable to a group of patients employed, for example, in an ammunition plant, a rubber factory or a fur-dyeing establishment; we have in mind rather the general run of patients encountered in every-day private and clinic practice.

Attempts to differentiate the vesicular palmar and plantar dermatoses by means of clinical criteria alone have not met with success. A few dermatologists maintain that while clinical differentiation is difficult it should not be entirely ignored, as it is by many. Scholtz,[2] for instance, who published a paper three years ago in which he dealt with the morphologic features of dyshidrosiform eruptions, remarked: "The diagnostic value of the morphologic differences between mycotic dyshidrotic lesions and those of systemic dyshidrosis has been generally underestimated by dermatologists and completely ignored by the protagonists of epidermophytids." He expressed the opinion that if more attention were given to the details of the clinical changes it might be helpful in arriving at a correct diagnosis. Varying opinions along the same lines of thought were expressed by Mitchell[3] of Chicago and Lehmann[4] of San Antonio. Mitchell said: "I do not pretend to be able to determine by inspection what is mycotic and what is not, and the only way this can be determined is by making strenuous efforts to find out whether they are mycotic."

2. Scholtz, Moses: Epidermophytids as a Clinical Conception, Arch. Dermat. & Syph. **25**:812 (May) 1932.

3. Mitchell, J. H.: Amycotic Dermatoses Simulating Ringworm and Erosio Interdigitalis Blastomycetica, Arch. Dermat. & Syph. **19**:659 (April) 1929.

4. Lehmann, C. F.: Acute Vesicular Eruptions of the Hands and Feet, Arch. Dermat. & Syph. **21**:449 (March) 1930.

Relative to this aspect of the subject, our own experience has effected a dubious attitude and guarded expression of opinion. We do believe, however, that the morphologic features of a dematophytid can be faithfully mimicked by lesions due to almost any number and variety of irritants, both exogenous and endogenous, and that when the patient who presents a vesicular eruption on the hands of indeterminate and obscure cause happens also to be afflicted with ringworm infection of the toes, then indeed is confusion worse confounded.

This brings us to the declaration of an opinion which we think is shared by the majority of dematologists in this country, namely, that it is futile to shut one's eyes to the fact that among the rank and file of practitioners the tendency to make false interpretations of these simultaneous eruptions on the feet and on the hands has become far too prevalent. To state the case bluntly, innumerable wrong diagnoses are constantly made and improper therapy is prescribed in cases of dyshidrosiform eruptions and have been ever since the "athletes' foot" propaganda came into its own, flourished and attained full bloom. The technic of many practitioners is to cast a glance at the vesicular eruption on the patient's hands and say to himself, "Ah! another case of ringworm infection," and then to the patient, "Let me see your feet. Yes, I thought so! You have ringworm of the feet, and the blisters on your hands are caused by the same parasite." This explanation is delightfully simple; all it lacks is confirmation.

It seems paradoxical, but is nevertheless true, that those who have the most experience with this class of dermatoses are those who require the most time to obtain the patient's complete history, to perform the essential microscopic and cultural investigations, to delve into the patient's atopic, allergic and immunologic status and to ascertain his response to various remedies—in short, to arrive at the correct diagnosis and prescribe the right remedy, as against making a wrong "snap" diagnosis and prescribing the wrong remedy.

Try as hard as we may, we find it difficult to refrain from quoting that hackneyed phrase about the medical pendulum, with its nasty habit of swinging either too much to the right or too much to the left. If one accepts the dictum of a number of authoritative observers who believe that between 70 and 90 per cent—even 100 per cent—of dyshidrosiform eruptions on the hands and feet exclusive of those definitely evoked by exogenous irritants originate from fungous infections, one has still to deal with a fairly conspicuous group of patients whose eruptions can be classed neither as contact dermatitis nor as fungous infection. This leaves one, figuratively speaking, with several stepchildren whose progenitors are either under suspicion or wholly unknown.

PRESENT STATUS OF DERMATOPHYTOSIS AND DERMATOPHYTIDS

Much progress from both a clinical and a laboratory standpoint has been made in the study of fungous diseases within the last decade. Additions to the knowledge have been the burden of numerous communications in the foreign and American literature. It might be well to take stock, to review these steps forward, to correlate the findings and to evaluate critically the new contributions.

For the purpose of this presentation it might be best to start with a brief review of the etiology, symptomatology and pathology of dermatophytosis and dermatophytids.

In the study of a large mass of material at the New York Post-Graduate Medical School and Hospital, the organisms most frequently encountered on the feet were Trichophyton gypseum, Trichophyton interdigitale and Monilia. Of course, numerous other species of Epidermophyton, Microsporon and Achorion were found, but they account for only a small percentage of the cases.

Fungi are ubiquitous. They live in the horny layer of the skin, and any factor or factors which favor maceration of the skin provide an excellent culture medium for the growth and propagation of the organisms. Moisture, and this is important from the standpoint of therapy, is therefore an outstanding contributory cause of fungous infection. It matters little whether the moisture is that of hyperhidrosis or of the bath, shower or swimming pool. The greatest opportunity for infection occurs wherever large groups of people meet and where insufficient prophylaxis against infection is taken, as at athletic clubs, gymnasiums and bath-houses.

The severity of the infection depends on many factors but primarily on the allergic response of the individual person to his infection. Of this we shall have more to say later.

The clinical appearance of tinea of the hands and feet is well known. There are the white, sodden epidermis, most frequently encountered between the fourth and fifth toes, the vesicular and bullous lesions found especially on the palms and soles and on the lateral surfaces of the fingers and feet, and the erythematous, dry, fissured, scaling eczematous areas found on both the hands and the feet. The hyperkeratotic type occurs less frequently. In tinea of the feet the toe-nails are most often involved, and any nail which lacks luster, even though it appears normal otherwise, will probably yield fungi on microscopic or cultural examination. Nails which are deformed, which show alterations in color or which present such changes as subungual hyperkeratosis are frequently involved. The infected toe-nail is said to play a not inconsiderable rôle in the production of recurrences.

The histopathology of dermatophytosis and of the dermatophytids is the histopathology of eczema. There are no tinctorial, morphologic or cellular changes which differ from those found in eczema.

In a great percentage of cases in which both the hands and the feet are involved and in which diligent search, both microscopic and cultural, is made, one finds no causative organism in the lesions on the hands. This fact led Williams to suggest that in such cases one is dealing with dermatophytosis of the feet and dermatophytids of the hands, hematogenous lesions of an allergic nature secondary to the primary lesions on the feet. These ids find their analogy in the trichophytid which appears in deep tinea infection, such as kerion, and also in the tuberculids. In 1929 Peck published experimental proof of Williams' original observation. By infecting the toes of previously unaffected persons and producing trauma by friction between the toes he caused vesicular eruptions to appear on the hands which were typical "ids." The hands appear to be a *locus minoris resistentiae* for the development of these secondary lesions.

The development of the trichophytid depends primarily on two factors, namely, (1) altered reactivity of the skin, i. e., allergy, and (2) the dissemination of the fungi or their products, or possibly both the fungi and the products combined, to the site of the "id." The altered reaction of the skin to fungi and their products is the allergy of infection, and for the sake of clarity we shall compare it with the immunologic reactions in another disease, tuberculosis. This altered reactivity depends on previous infection with fungi, and it can be demonstrated by the intradermal injection of toxins from fungi (trichophytin). This is analogous to the first infection with the tubercle bacillus and the demonstration of altered reactivity by the injection of tuberculin. This altered reactivity of the skin is responsible for the appearance of the "id," for the trichophytid (or moniliid) is the result of an inflammatory response of the skin to the trichophytic (or Monilia) antigen.

In any discussion as to whether the "id" is due to the fungi or to their products (or to both), one is treading on debatable ground. Bloch was able to produce lesions resembling "ids" in animals by the injection of trichophytin. Jadassohn grew fungi repeatedly in cultures of the blood of cutaneously infected animals. These cultures, however, gave positive results in the early postinfectious period, and the fungi might have been forced into the blood stream by mechanical means. Sulzberger continued this work and demonstrated that a second phase, with numerous positive cultures of the blood, followed the first, postinfectious, phase with its succeeding negative phase. It is probable that the appearance of the "id" is coincidental with an infection in the blood stream with fungi from the feet. There is added proof in the occasional

positive culture of the blood reported for human beings. Ambrosoli reported 2 positive cultures of 1,269 in a study of 700 cases of trichophytic disease. The difficulties in obtaining positive cultures of the blood in sporadic specimens of a limited quantity of blood must be obvious.

In this connection we call attention to the work of Ayres and Anderson. These authors were able to show that from 4 to 8 per cent of serum from a person with true "id" when incorporated in Sabouraud's medium will inhibit the growth of fungi isolated from the primary lesion. This does not hold true for Cryptococcus, pleomorphic forms of Epidermophyton or Monilia, nor does it hold true in instances of eruptions on the hands which are due to irritants, hypersensitivity or local infection with fungi. This work, if confirmed, will add a helpful test to the armamentarium of the dermatologist in the differential diagnosis of dyshidrosiform eruptions.

### CHEIROPOMPHOLYX

*Present Status.*—From the standpoint of pathogenesis and histopathology it is believed by the great majority of modern dermatologists that true palmar and plantar dyshidrosis, i. e., an eruption caused primarily by a disorder of the sweat apparatus in these regions, does not exist. (Such conditions as sudamina, miliaria crystallina and hydrocystoma do not fall into this category and are not pertinent to the present discussion.)

The subject of cheiropompholyx was recently discussed in extenso in two articles in the *British Journal of Dermatology and Syphilis* by McLachlan and Brown [5] and Muende.[6]

In a series of cases which they studied the first-named authors found that "approximately 15 per cent of cheiropompholyx eruptions belong to the eczema, asthma and hay-fever group, and that there is a definite hereditary predisposition to eruptions of the allergic type."

A typical example was reported in a case of a woman aged 27.

The patient suffered from urticaria, off and on, all her life. In addition she had two or three attacks of angioneurotic edema. She had also suffered, during her twenties, from attacks of cheiropompholyx with typical sago-grain vesicles. The family history is as follows: Maternal grandmother suffered from eczema. Her paternal uncle suffered from asthma, and her paternal great-grandfather from hay-fever. The patient herself is subject to urticaria, angioneurotic edema, bilious attacks after partaking of certain food, dysmenorrhea and finally cheiropompholyx.

5. McLachlan, A. D., and Brown, W. H.: Cheiropompholyx, Brit. J. Dermat. **46**:457 (Nov.) 1934.

6. Muende, I.: Cheiropompholyx, Brit. J. Dermat. **46**:479 (Nov.) 1934.

The authors cited several cases in which more than one member of an atopic family group suffered simultaneously from this eruption, and they stated the belief that the inborn hereditary factor has been overlooked in cases of cheiropompholyx and that they had enough evidence to justify them in pointing out its importance.

With this point of view we are in full accord. We have had the opportunity to observe two members of a family and, in one instance, a neurotic mother and her two neurotic daughters who had vesicular eruptions of the palms and lateral surfaces of the fingers and in whose cases the diagnosis of contact dermatitis, primary local fungous infection, trichophytid, moniliid or idiopathic eczema did not seem to be applicable, despite the great latitude in the choice of diagnosis in such cases. Peck, in his paper on dermatophytosis, mentioned conditions which he could not classify under the head either of dermatophytid or of eczema and which he thought might be examples of true dyshidrosis. A still greater latitude in the field of clinical diagnostic excursions has been made available by the assumption that bacteria, acting either exogenously or endogenously, are capable of producing similar dyshidrosiform eruptions, as well as "bacteriids," in a sense analogous to mycosids and tuberculids. However, a number of observers, among whom are Sabouraud, Whitfield, Sicoli and Scholtz, still adhere to the conception of cheiropompholyx as a clinical entity of nonparasitic nature.

We have had 2 patients under observation in whom the ingestion of orange juice evoked vesicular lesions resembling sago grains on the palms and fingers. Manual contact with oranges or orange juice, the existence of ringworm, infection with Monilia and eczema could be fairly definitely ruled out. The eruption simulated trichophytids. Thus one is constrained to recognize that certain dyshidrosiform eruptions are at times encountered which apparently do not lend themselves to classification with contact dermatitis, local fungous infections, mycosids, bacteriids and "eczema." Notwithstanding the fact that the histopathologic changes in this group are practically identical with those occurring in dyshidrosiform eruptions of known etiology and despite the almost universally accepted view that disorders of the sweat apparatus are not causative factors, one is apparently still confronted with a condition to which the name cheiropompholyx has clung since 1871.

It is of interest to note that both Jadassohn and Darier have placed this condition in the category of eczema, a classification which the majority of British dermatologists regard as unsatisfactory. While it seems to us that the arguments in favor of the individuality of pompholyx are propounded by implication rather than by analysis, we still believe that the moment to drop the term pompholyx from the nomenclature has not arrived.

*Pathogenesis.*—McLachlan and Brown [5] lay considerable stress on neurogenic and endocrine-sympathetic factors in the etiology of cheiropompholyx. They stated:

These causal factors have been noted by comparatively few writers, and seem to have been neglected. We would like to draw attention to their importance, for they occupy a definite place in our series. Nervous influences in relation to diseased states have within recent times become accepted as important aetiological factors, particularly in certain dermatoses, e. g., neuro-dermatitis, alopecia, urticaria, eczema, etc., and there is every reason for believing that there is a neurogenic factor in certain cases of cheiropompholyx. The suddenness of onset is in itself suggestive of a nervous cause. Tilbury Fox records the probability of a nervous factor in cheiropompholyx, stating that "some patients were prostrated with mental anxiety and worry and were speedily exhausted." Becker, in his article on dermatoses associated with neuro-vascular instability, mentions neurogenic dyshidrosis, and says the nervous factor has been overlooked; O'Donovan observes that cheiropompholyx is often seen after nervous strain, worry or shock, while Martin from a personal experience emphasizes this point. In several of our cases the nervous element was the dominant one. In one case especially, which was under observation for twelve years, the nervous factor was particularly evident. The patient was a telephone operator, very nervous and highly strung, who stated emphatically that the eruption originally started after a local injury by a telephone wire, but that the subsequent attacks were associated with worry or nervous strain. Another case which may be cited is as follows:

Female, aged 15 years, dispatch girl. Thin and exhausted looking, and definitely neurotic in type. She states that previous to the onset of the eruption she had been extremely busy, and had worked after hours for many weeks. She exhibited a very decided tremor in both hands, and her reflexes were all exaggerated. She suffered from headaches and sleeplessness. No fungus was found, and no other evidence to account for her condition.

The association of cheiropompholyx with endocrine disturbances is difficult to assess, but the relationship between the two has been so close in a number of instances that it cannot be ignored. This has been commented upon by other writers. Pregnancy, menstruation and the menopause coincided with the attacks in 21 of our cases.

In several cases the attacks followed within 2 to 4 weeks of parturition, and in others were closely related to the menstrual period, or originated about the menopause. Lehmann recalls a case recurring a few days before each period, especially in hot weather. Further evidence of endocrine disturbance or the nervous factor is found in two patients who showed definite enlargement of the thyroid gland with a slight degree of exophthalmos, and in one case a very decided goitrous family history. The goitrous factor has been commented upon by Wile, who records a group of cases of non-parasitic cheiropompholyx clinically indistinguishable from ringworm. Living in the great goitre belt, he found many cases associated with exophthalmic goitre, which inclined him to believe that they were of neurogenic origin.

Among other modern investigators, Muende [6] has upheld the conception of true dyshidrosis as a disease entity. In tabulating the funda-

mental signs and symptoms he adopted those propounded and agreed on by both Hutchinson and Fox. We quote Muende as follows:

1. The rash is preceded by a sense of increased discomfort in the parts to be affected.

2. The eruption then appears spontaneously and symmetrically on both hands without any antecedent erythema; has somewhat deeply placed minute flattish vesicles, which resemble sago-grains, embedded in the skin.

3. These vesicles appear scattered, at times irregularly, but at others in small groups along the sides of the fingers and also on the palms.

4. In severe cases these vesicles may coalese to form large bullae.

5. The eruption undergoes spontaneous resolution without rupture of the vesicles, and

6. The condition tends to recur.

If we adhere rigidly to this description, as indeed we ought, when discussing a case of cheiropompholyx, it will soon become evident that the disease cannot be attributed to eczematous eruptions of exogenous origin, or wholly to infection with organisms, either mycotic or bacterial.

Muende expressed the opinion that there is a group of vesicular eruptions in which an infective origin cannot be incriminated nor can any exogenous or definite endogenous factor be observed. Sweating need not be a special feature in these cases, nor are the attacks related to hot weather. The patients are usually worried and overworked, but Muende did not care to suggest the mechanism producing the eruption.[6]

Rajka and several French writers have described cases of eruptions due to infection with the streptococcus or the staphylococcus, but the eruptions had no resemblance to true cheiropompholyx, corresponding rather to vesicular dermatoses caused by coccic-infection.[6] We have examined patients who had vesicular eruptions on the hands, the clinical course and appearance of which seemed to justify the diagnosis of pompholyx rather than any other designation. Some of these eruptions might be due to sensitization to various foods or to such drugs as iodine and the salicylates.

From the foregoing statements the inference may be drawn that before the description of trichophytids and moniliids—particularly of the palmar surfaces—pompholyx, as the name is interpreted in this country, had been recognized as a disease entity of nonparasitic nature. In England the name cheiropompholyx is applied to palmar and plantar vesicular eruptions in general, with qualifying adjectives, such as fungous, toxic, parasitic and nonparasitic. In American textbooks, even in those published within the past year, pompholyx is described as a nonparasitic disease.

Since the facts regarding the allergic manifestations of the superficial mycoses, especially those expressed by vesicular palmar eruptions, have become generally known to American dermatologists, pompholyx has existed in what might be called a state of suspended animation.

### DIFFERENTIAL DIAGNOSIS

If one assumes that efforts at purely clinical differentiation are of little practical value save in exceptional instances and that the most painstaking questioning of the patient with respect to external contacts, sensitization to certain foods and drugs, his occupation or profession, and his hobbies or participation in sports and games of various kinds offers no clue to possible etiologic factors, one has recourse to the following diagnostic procedures:

1. One can search for the causative factor by means of patch tests, to determine epidermal sensitization to one or several allergens with which the patient might come in contact. Not only is this procedure applicable in cases of trade eczema and occupational dermatitis, but, as has been demonstrated,[7] it may prove of value in identifying conditions suspected of being trichophytids. In certain cases of ringworm infection a patch test with trichophytin resulted in a reaction of the eczematous type, and histologic examination of these reactions showed typical spongiosis and intra-epidermal vesicles. This proves that products of fungi may elicit eczematous eruptions in hypersensitive skin in the same manner as do innumerable substances that play a causative rôle in industrial dermatoses. In children below the age of 5 years, in whom infection with Epidermophyton is comparatively rare in our experience, the patch test with trichophytin would seem to be of considerable diagnostic value. Unfortunately, from the practical standpoint the test does not hold good in adults on account of the widespread incidence of epidermophytosis of the feet in the adult population.

2. One can search for the causative factor by means of intradermal tests with extracts of trichophytin and oidiomycin. As pointed out by Jadassohn, by Bloch and his pupils and by many other investigators, this test is also of only limited diagnostic value for the reasons previously mentioned with respect to the patch test. The same limitations apply to the tuberculin test. It has been demonstrated [8] that oidiomycin, the extract of Monilia albicans, in the majority of patients causes a positive intradermal reaction of the late papular type analogous to that evoked by trichophytin and tuberculin. There exists a sharp immunologic separation between hypersensitivity to trichophytin and hypersensitivity to oidiomycin, for sensitizations caused by the Monilia group and those caused by the Epidermophyton group seem to be specific for each group and are not immunologically related. Despite these indi-

7. Sulzberger, M. B., and Lewis, G. M.: Trichophytin Hypersensitiveness Demonstrated by Contact Tests, Arch. Dermat. & Syph. **22**:410 (Sept.) 1930.

8. Kerr, P. S.; Pascher, F., and Sulzberger, M. B.: Monilia and Trichophyton Extracts: Their Combined Use in Eczematous Ringworm (Dermatophytosis and Dermatophytids), J. Allergy **5**:288 (March) 1934.

vidual specific reactions, the tests are of only limited value in adult patients with dyshidrotic eruptions, but they should prove of considerable value in cases of vesicular eruptions of the hands and feet in young children. It has been demonstrated that most persons possess a cutaneous hypersensitivity to oidiomycin and that some patients who have no evidence of present or past eruptions caused by Monilia exhibited a high degree of hypersensitivity to intradermal injections of oidiomycin. Therefore, as is the case with trichophytin and tuberculin, the reaction to the oidiomycin test is not diagnostic. It is possible that with improvements and refinements in the technic of performing the tests, in the preparation of the test solutions, in the interpretation of the character and degree of reactions with standardized high dilutions of different titers on different parts of the body and on previously diseased skin, these tests will ultimately prove their worth in differential diagnosis. While we realize the import of a flare-up of localized lesions following the injection of antigens, we have not had sufficient experience to be able to estimate the significance of such a reaction.

3. One can search for the etiologic agent by microscopic examination for fungi in the affected areas. Fungi may be found in a large proportion of cases of mycosis of the feet, if not on the first search, possibly after repeated efforts. Since the majority of patients have used antiseptic and keratolytic applications on the feet before consulting their physician, they are advised to apply wet dressings of saline solution to the affected parts for several days before a fruitful microscopic search can be undertaken.

In patients presenting simultaneous eruptions on the feet and hands the vesicular lesions of the hands practically always prove to be free from organisms and are therefore manifestations of an allergic state of the skin, clinically and immunologically documented as trichophytids or moniliids or perhaps both.

Occasionally a case is met in which fungi can be readily demonstrated in large numbers in dyshidrotic lesions on the hands. These lesions are manifested by primary local ringworm infections of the hand, analogous to those of the feet. Peck [9] has called attention to the fact that such a primary local dermatophytosis of the hand is capable of producing a dermatophytid of the feet, thus reversing the usual course of events in the sensitized patient.

In the search for fungi from the lesions between and on the toes, and from affected toe-nails, it should be remembered that specimens are best obtained from the peripheral portions of the lesions and that vesic-

9. Peck, S.: Epidermophytosis of the Feet and Epidermophytids of the Hands, Arch. Dermat. & Syph. **22**:40 (July) 1930.

ular lesions in the immediate vicinity of the primary process may prove to be sterile and are therefore trichophytids, analogous to those on the hands (Williams [1]).

4. Cultural investigations may be carried out. These require an expert mycologist and a good laboratory.

5. By means of biochemical investigations, Marchionini [10] attempted to show that by testing the hydrogen ion concentration of the contents of the vesicles, he was able to distinguish between the true dyshidrosis of Tilbury Fox and the dyshidrosiform eruptions of parasitic or toxic origin. He found that in cases of true dyshidrosis the hydrogen ion concentration of the fluid of the vesicles is 5, the same as that of sweat. In cases of dyshidrosis of mycotic origin the hydrogen ion concentration is 7 (neutral), while in cases of epidermophytids and dyshidrosiform eczema the hydrogen ion is from 7.2 to 8.2 (frankly alkaline). Marchionini admitted that his method is too complicated for every-day routine practice and in lieu of it advocated the use of litmus paper to test the reaction of the fluid of the vesicles. Litmus paper changes color at about hydrogen ion concentration 6.8. In the early stages of true dyshidrosis, the author stated that a definite change from blue to red takes place, owing to retained sweat from the eccrine sweat glands. The contents of the vesicles of infectious dyshidrosis are said to produce an amphoteric reaction, while the contents of vesicles of other dyshidrosiform eruptions, eczema and allergic epidermophytid change red litmus paper to blue. On the strength of these observations Marchionini voiced his opinion emphatically in favor of the conception of true dyshidrosis of Tilbury Fox as a disease sui generis.

As McLachlan and Brown aptly stated, these findings call for further investigation and confirmation.[5]

6. Inhibition of growth of fungi, as described by Ayres and Anderson, has already been mentioned. This procedure should be thoroughly investigated.

7. The therapeutic test is helpful. It has been stated by several authors that the secondary "id" eruption clears up when the primary focus of infection is eliminated. Would that that were true! Unfortunately, practical experience has demonstrated that the "id" eruption may, and often does, persist long after all traces of the primary infection have vanished. In this connection, Williams has stressed the necessity of excluding the nails as a potential depot of persistent dissemination of the fungi.

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10. Marchionini, A.: Pathogenesis and Differential Diagnosis of Dyshidrotic and Dyshidrosiform Diseases of the Hands and Feet, Dermat. Ztschr. **58**:222 (May) 1930.

With respect to a therapeutic test by means of desensitization, we cannot estimate the value of this method until we have had a great deal more experimental clinical material on which to base definite conclusions. We, as well as a number of other observers, have obtained what appeared to be very good results in selected cases of recalcitrant ringworm and infection with Monilia. We believe that with desensitization procedures the future holds in store an efficient and reliable mode of therapy. Perhaps an important phase of the procedure is to make sure that one is using the extract or extracts derived from the actual infecting organism, in contradistinction to the indiscriminate use of "shotgun" vaccines. In all events, the method deserves a thorough and carefully controlled trial. One of the reasons that the reaction to this therapeutic test is difficult of evaluation is that so few patients are willing to submit to inoculations for desensitization without at the same time employing topical remedies of one kind or another. In our opinion, the use of topical remedies, no matter how bland they may be, vitiates the therapeutic test. Furthermore, the eruption is likely to undergo remissions and recurrences, and spontaneous cure may result.

A therapeutic test based on response to roentgen and ultraviolet irradiation and other forms of radiation therapy may have value. With this mode of treatment we have had too few controls to justify an assumption of definite conclusions. We have the impression that response to radiation therapy is at best an uncertain and rather intangible factor in diagnostic differentiation; it will not bear comparison with the therapeutic test of a plaque of mycosis fungoides or a round cell sarcoma, for example, in which roentgen rays are utilized as a test of therapy in the absence of microscopic observations.

## SUMMARY AND CONCLUSIONS

1. In the United States the majority of vesicular eruptions of the hands in adults, exclusive of occupational eczema, dermatitis venenata and eczema of unknown cause, are accompanied by fungous infections of the feet. Such eruptions on the hands are usually epidermophytids, moniliids or trichophytids.

2. Owing to the fact that a large proportion of the adult population in this country has, or has had, fungous infection of the feet, positive reactions to the intradermal and patch tests with trichophytin and oidiomycin are of little significance in their direct bearing on the differential diagnosis of a coincident vesicular eruption on the hands.

3. The significance of focal, local and general reactions following the intradermal injection of extracts of fungi cannot at present be properly appraised with respect to vesicular dermatoses of the hands and feet.

4. The mere fact that a patient has a vesicular eruption on the hands and a coincident eruption on the feet does not indicate that the eruption on the hands is necessarily or presumably an "id," due to dissemination of fungi or their products (or possibly both) from the original focus on the feet. The eruption on the hands may be caused by a number of demonstrable agents other than fungi, or it may be evoked by a wholly unknown agent.

5. To differentiate these eruptions, a careful history must be obtained from the patient.

6. The diagnosis of "ids" should not be entertained without strongly corroborative evidence, the most important of which is the demonstration of the causative organism, either microscopically or by culture, from the focus of primary infection of the skin or nails.

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# II. EFFECT OF VARIATION OF RATIOS OF DEXTROSE TO PEPTONE ON COLONIES OF CERTAIN PATHOGENIC FUNGI

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In a previous paper [1] observations relative to culture mediums for pathogenic fungi, features of importance in the development of a suitable medium and the effects on the morphology of the colony of the variation of the ratio of peptone to dextrose were considered. In this paper, under series 2, a comparison of growths on peptone, proteose peptone or tryptone and dextrose of varying ratio is made, and the importance of physical chemistry in the determination of the morphology of the colony is discussed.

In series 2 the following pathogenic fungi and the two nonpathogenic saprophytes Lichtheimia sp. and Scopulariopsis brevicaulis were studied: Achorion Schoenleinii, Acladium Castellani, Candida candida, Endodermophyton tropicale, Endomyces capsulatus, Endomyces dermatitidis, Epidermophyton cruris, Epidermophyton inguinale, Geotrichum Bachmann, Glenospora Gammeli, Indiella americana, Microsporon Audouini, Microsporon felineum, Microsporon gypseum, Monosporium apiospermum, Monilia albicans, Oospora humi, Sporotrichum Schenckii, Trichophyton crateriforme, Trichophyton granulosum, Trichophyton gypseum-asteroides, Trichophyton gypseum-lacticolor, Trichophyton interdigitale, Trichophyton japonicum, Trichophyton niveum, Trichophyton sulfureum and Willia anomala.

## SERIES 2

A comparative study was made of growths on peptone, tryptone and proteose peptone in an effort to decide which medium is superior. The same abbreviations are used as were used in the former paper,[1] together with T indicating tryptone and P indicating proteose peptone. The following mediums were used: S, W, L and R (1, 4, 8 and 12

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1. Williams, J. W.: I. Effect of Variation of Ratios of Dextrose to Peptone on Colonies of Certain Pathogenic Fungi, Arch. Dermat. & Syph. **32**:893 (Dec.) 1935.

per cent peptone, respectively); ST, WT, LT and RT (1, 4, 8 and 12 per cent tryptone, respectively); SP, WP, LP and RP (1, 4, 8 and 12 per cent proteose peptone, respectively, to which was added 4 per cent dextrose); ST1, WT1, LT1 and RT1 (1, 4, 8 and 12 per cent tryptone, respectively, to which was added 1 per cent dextrose); ST4, WT4, LT4 and RT4 (1, 4, 8 and 12 per cent tryptone, respectively, to which was added 4 per cent dextrose); SP1, WP1, LP1 and RP1 (1, 4, 8 and 12 per cent proteose peptone, respectively, to which was added 1 per cent dextrose), and SP1, WP4, LP4 and RP4 (1, 4, 8 and 12 per cent proteose peptone, respectively, to which was added 4 per cent dextrose). By peptones is meant peptone, proteose peptone and tryptone.

Difficulty was encountered with the higher concentrations of proteose peptone because of the failure of the mediums to solidify. Therefore, observations on RP1, RP4 and LP4 are often omitted. Another difficulty with this medium was the depth of color, which was often imparted to the growth and which obscured any organismal pigment that might be present.

For convenience the groupings used in series 1 are followed in this paper.

GROUP A

*Achorion Schoenleinii.*—As the concentration of peptone, tryptone or proteose peptone is increased, the growth becomes more radiate, cratered and irregular. As the concentration reaches 8 and 12 per cent, the growth begins to appear wet in certain areas. The growth is slightly greater on 8 and 12 per cent concentrations than on 4 per cent concentration and are considerably greater than on 1 per cent concentration. It is probable that the best growth is that on 4 per cent tryptone, and the next best growth is on 8 and 12 per cent proteose peptone and 8 per cent peptone.

When 1 per cent dextrose is added to the peptones, the culture on ST1 shows a dainty growth with twenty radii centrally, while the center of the growth on WT1 shows cracking and the edges are heaped up. On SP1 there are irregular radii and cratering centrally, with cracking, giving a granular appearance. On WP1 the central cracking is coarser and the edges are more heaped up than on ST1, WT1 and SP1. On W1 the growth is larger, and there is more white powder and the growth is more irregular centrally than that on P1. The growths on the peptones in higher concentrations seem to show more aerial mycelium and become, although more irregular, more pleomorphic. The growths on tryptone and proteose peptone seem to be best differentiated. On SP1 and ST1 there is a suggestion of pink.

When 4 per cent dextrose is added to the peptones, the growths on S4 and ST4 show some buff color and powder and are better differentiated than those on other mediums. With a higher concentration of peptone the growths either are too wrinkled or acquire aerial mycelium and become pleomorphic. On the peptones in higher concentration than 1 per cent and on 4 per cent peptone the differentiation of the growths is 3+. Tryptone causes the best differentiation of the growth.

*Epidermophyton Cruris.*—A fawn-colored powder is more apparent on peptone and proteose peptone than on other mediums. The growths on the 8 per cent concentrations of each of the peptones show more marked cratering, more powder and a more heaped-up edge than those on other concentrations. The growth on WR shows as pronounced change as that on LT or L. The growth is small until the concentration of peptone reaches 8 per cent, except on the 4 per cent proteose peptone.

When 1 per cent dextrose is added to the peptones, the growth on W1 reveals an amber-colored base and a brownish-yellow tinted powder on some plants and is slightly cratered with a few radii. On P and R the changes on the addition of 1 per cent dextrose are less regular than those on W1, but they are marked. There is a tendency for the powder to be light pink on L1.

When 4 per cent dextrose is added to the peptones, there is more pleomorphism, especially on 1 per cent peptone. The growths on the other concentrations are not especially characteristic. Pleomorphism seems to decrease with an increase in the concentration of peptone. Powder varying from yellow to lemon is present, especially on WT4 and WP4.

*Indiella Americana.*—The growth on S4 is light olive-green, radiate and of doeskin variety and is by far the most typical. With an increase in the concentrations of peptone there is a tendency to frosting, nodular appearance, spicules and pleomorphism. As on S4, the growth on SP4 is light olive-tan, but it does not show the regularity of that on S4. On S1 the growth is white but shows good differentiation. The growths on RP1 and RT1 look like fur on a teddy-bear. The growth on W4 shows a wrinkled cream-puff appearance centrally. The extent of the growth seems to increase with the concentration of peptone and dextrose.

*Microsporon Felineum.*—The growths on the peptones in various concentrations are fawn-colored. On 1 per cent peptone the growth is somewhat scant, but on higher concentrations the growths take on the appearance of doeskin. On 8 and 12 per cent concentrations of the peptones the growths are more radiate and less pleomorphic than those on mediums of lower concentration.

On the addition of 1 per cent dextrose, the growth on W1 shows some of the appearance of doeskin, is wrinkled and has many radii. The growth on W1 and that on RT1 are very good; the latter has a brownish color. The growths have a color varying from yellow to cream.

On the addition of 4 per cent dextrose, the growth on R12 has a skinlike appearance and shows better differentiation. In these observations the ratio of dextrose to sugar seems important. The growth is yellowish and cream-colored. The best differentiation is found in the growths on the peptones. There is more growth on proteose peptone. Pleomorphism decreases with an increase in the concentration of peptone and a decrease in the concentration of sugar.

*Monosporium Apiospermum.*—Only the growths on peptones in a concentration of 1 per cent show the typical white mycelium (thin film). On W and WT there are radii. As the concentrations of peptones are increased, there is an increase in frosting, in the granular and glassy appearance, in the spicule-like mycelium and in waxiness. On R the glassy, beeswaxy growth appears as though meshed, or mitered together. On the addition of 1 per cent dextrose, there appears a white film of mycelium, which becomes scant and the growth is heaped up and wrinkled. When the concentration of the peptones is increased over 1 per cent the previously described characteristics usually give way to a granular frosted

surface, waxiness and stubble mycelium, these being superseded, with an increase in concentration, by a waxy surface. There are black areas at the base.

On the addition of 4 per cent dextrose, there is more white mycelium, but this gives way to waxy and frosted areas (even on 1 per cent proteose peptone) with an increase in the concentration of the peptones. Generally, the growth of this organism seems to increase with an increase in the concentration of the peptone and dextrose (except on 4 per cent dextrose and tryptone, where it decreases), and waxiness increases with an increase in the concentration of the peptones, especially on proteose peptone. A decrease in the concentration of dextrose is also important. Blackening of the base is apparent on 1 per cent concentrations of the peptone.

*Trichophyton Crateriforme.*—Growths of this organism are comparatively good on all mediums. They are too wrinkled when the concentration of peptone is 8 or 12 per cent and when dextrose is not added to the 1 per cent concentrations. The growths on peptone and tryptone are superior to those on proteose peptone. There is no growth on RT4.

*Trichophyton Granulosum.*—On 1 per cent concentrations of the peptones the growths are mycelial. On 4 per cent and higher concentrations of the peptones there is a tendency for a portion of the growth to become bare of mycelium and even to appear waxy, so that on 12 per cent proteose peptone and 12 per cent tryptone peptone the growth becomes like a collapsed, crinkled cream puff, giving the appearance of the endodermophytons on W1.

When 1 per cent dextrose is added to the various concentrations of the peptones, the white mycelium becomes slightly diminished with an increase in the concentration. On L1 and R1 there are concentric rings in the growth, while on W1 the rings are suggested. An increase in the concentration of proteose peptone causes a tendency for the growth to become bare of mycelium, to produce more powder and to become more wrinkled. This effect is seen to a greater extent on an increase in the concentration of tryptone.

As the concentration of the peptones is increased and that of dextrose is decreased, the growths tend to lose their aerial mycelium.

When 4 per cent dextrose is added to the medium, the growth becomes successively less pleomorphic and shows wrinkling, radii and powder. With an increase in the concentration of the peptones the growths become less mycelial on all mediums.

As the concentration of the peptones is increased and that of dextrose is decreased, the growths tend to lose their aerial mycelium and become more wrinkled and radiate; on RT1 they even become granular.

*Trichophyton Gypseum-Asteroides.*—The growths on the 1 per cent concentrations of the peptones are mycelial. Except on proteose peptone, on which the growths are irregular, the growths on the remaining concentrations show cratering, wrinkling and powderiness. The growths on W, L and WT are probably most typical.

When 1 per cent dextrose is added to 1 per cent concentrations, the growths are mycelial. With an increase in the concentration of peptone the growths become successively less mycelial, that on W1 showing more cratering and that on L1 much less mycelium. The growths on proteose peptone are irregular. The growth on WT1 shows cratering, with radii, and those on LT1 and RT1 show less mycelium and a more wrinkled and radiate effect.

When 4 per cent dextrose is added to peptones of 4 per cent or higher concentration, there are powderiness and an increasing tendency to cratering and

wrinkles; there is a marked decrease in the growth on LT4, and there is no growth on RT4. There is a faint orange powder on L4.

*Trichophyton Gypseum-Lacticolor.*—As the concentration of peptone is increased, there is a tendency to an increase of powder, cratering, wrinkling and radii. The growths on 8 and 12 per cent concentrations of the peptones show the greatest differentiation.

On the addition of 1 per cent dextrose, the growths, although slightly cratered on the 1 per cent concentrations of the peptones, become more cratered, less mycelial and more powdery. Mediums of 8 and 12 per cent concentration of the peptones seem the more suitable.

On the addition of 4 per cent dextrose, the growths on 1 per cent concentrations of the peptones show marked mycelial development, the growths become cratered, powdery and wrinkled with an increase in the concentration of peptone. There is an orange tint on R4.

*Trichophyton Interdigitale.*—On the various peptones there is more marked differentiation with an increase in the concentration. The development of the growths on mediums of the next higher concentration of proteose peptone and tryptone seems to correspond more closely with that of the growth on peptone. A concentric band with a few radii appears on L, and cratering and some powder are noted on R.

On the addition of 1 per cent dextrose and with an increase in the concentration of the peptones over 1 per cent, the aerial mycelium is gradually lost and the growths become powdery, showing wrinkling, cratering and a brownish tint.

On the addition of 4 per cent dextrose, there is a great increase in aerial mycelium on the 1 per cent concentrations of the peptones, which becomes less with an increase in the concentration, with knobbing, cupping, at times radii and a cream-colored tint, except on tryptone, on which there is a pink tint.

An increase in the concentration of peptone and a decrease in that of dextrose causes a decrease of mycelium and an increase of powderiness, radii and wrinkling.

*Trichophyton Niveum.*—On RT there is a platter-like growth with an amber-colored edge. On the peptones in 1 per cent concentrations, the growths are pleomorphic, becoming less pleomorphic as the concentration of peptone is increased and showing powder, frosting at the edge, wrinkling and cratering.

On the addition of 1 per cent dextrose, some cratering becomes apparent on 1 per cent peptones, but the cratering increases together with radii and irregularity, with an increase in the concentration of peptone.

On the addition of 4 per cent dextrose, there is a suggestion of pink on SP4; on 1 per cent peptones there is considerable pleomorphism, which decreases with an increase in the concentration and is accompanied by cratering, wrinkling and radii. On RT there is no growth. The growths seem to increase in amount with an increase in the concentration of sugar.

*Trichophyton Sulfureum.*—The mycelium is irregular. On R there is a powdery and slightly cratered growth, with a creamy tint; that on RP is somewhat similar. The growths on these mediums are better differentiated. The growths on tryptone seem to have more mycelium, those on LT being better developed.

On the addition of 1 per cent dextrose, the mycelium seems to increase with an increase in the concentration of peptone. It is probable that the better mediums are those of 1 per cent concentration of the peptones.

On the addition of 4 per cent dextrose, the 1 and 4 per cent concentrations of the peptones are probably the best mediums.

Development and pleomorphism seem to increase with an increase in the concentration of peptone and sugar. The growths at least suggest the sulfur tint, which varies.

GROUP B

*Epidermophyton Inguinale.*—W and WP are the best mediums, with powder from fawn to light yellow, and with cratering and radii. On R there is a tint of pink. High concentrations cause too much wrinkling, and pleomorphism occurs on proteose peptone.

On the addition of 1 per cent dextrose, the growths on 4 per cent concentrations of the peptones show the better differentiation, but the differentiation is also good on the 1 per cent concentrations. Changes are more marked on proteose peptone than on other mediums. Amber and yellow pigment are noted.

On the addition of 4 per cent dextrose, the growths become more pleomorphic and more wrinkled as the concentration of peptone is increased, with the exception of those on proteose peptone, on which pleomorphism apparently decreases slightly. There is amber pigment.

*Microsporon Audouini.*—The growths on 4 and 8 per cent tryptone are probably the best differentiated, with faint orange radii and slight sinking of the plant centrally; the growth on 4 per cent petpone is next best. On the addition of 1 per cent dextrose the growths on peptone are better, those on L1 being best and those on LT1 and LP1 next best. All show coloration from light orange to tan. An increase in the concentration of peptone to R1 seems to increase the mycelium, while a decrease in the concentration from 8 per cent results in somewhat less differentiation.

On the addition of 4 per cent dextrose to 1 per cent peptone, a beautiful orange-colored growth results, with low mycelium; as the concentration of peptone is increased, there are apparently more powder and wrinkling. The growths on proteose peptone and tryptone are more mycelial than those on the aforementioned mediums, and there are no growths on the 4, 8 and 12 per cent tryptone.

*Microsporon Gypseum.*—On the peptones the pigmentation ranges from tan to salmon; on 4 per cent peptone, 4 per cent proteose peptone and 8 per cent tryptone there seems to be better differentiation of the growths, with well defined radii, wrinkling and comparative freedom from aerial mycelium.

On the addition of 1 per cent dextrose, the growths on 4 and 8 per cent concentrations of the peptones show up well, with a powder from orange to tan and radii toward the center, with some wrinkling.

On the addition of 4 per cent dextrose, there is more mycelium, which is reduced by an increase in the concentration of the peptone, but not sufficiently to make the growth as typical as those previously described.

*Trichophyton Japonicum.*—There are not many growths on the peptones without dextrose. There is more pigment on 4 per cent peptone and 4, 8 and 12 per cent tryptone and less pigment on proteose peptone.

On the addition of 1 per cent dextrose there is more growth, a yellow tint being apparent on the growth on 1 per cent peptone, with little discoloration of the medium; on an increase in the concentration of peptone the browning of the medium becomes more intense. On proteose peptone there is less browning and slightly less growth.

On the addition of 4 per cent dextrose there is more pigment, especially on 4 per cent peptone, with the growths on other concentrations showing less pig-

ment; wrinkling and cratering become marked in growths on higher concentrations of the peptones, especially of proteose peptone. The extent of the growth is increased on all mediums.

GROUP C

*Endomyces Capsulatus.*—The thin mycelium decreases with an increase in the concentration of peptone, and its place is taken by a coarser mycelium and progressively more frosting of fawn color. The growths are more profuse on proteose peptone and tryptone than on peptone; on proteose peptone in high concentrations the mycelium is especially matted, and on tryptone there appears a nipple-like base from which spicules extend, often covered with bits of white mycelium or attached to the adjacent glass by footlets.

With 1 per cent dextrose a somewhat similar appearance occurs with an increase in the concentration of peptone. On 1 per cent concentrations of the peptones the growths are white and mycelial, except on proteose peptone, where the growths correspond more to that on 4 per cent peptone. On all mediums with 1 per cent dextrose the growths are more profuse and assume the appearance of beeswax.

With 4 per cent dextrose the growth on 1 per cent peptone has a light fawn-colored mycelium at the center, with frosting around it; this formation is exaggerated, the mycelium becomes coarser and more matted and the frosting is greater as the concentration of peptone is increased. On 1 per cent proteose peptone there is white mycelium, but the extent of the growth quickly decreases as the concentration of proteose peptone is increased. There is no growth on RP1. On tryptone and peptone the growths seem to increase with an increase in the concentration of dextrose and tryptone or peptone.

*Endomyces Dermatitidis.*—On 1 per cent peptone there is an area of white mycelium centrally. On an increase in the concentration of peptone the mycelium becomes matted and spicules appear. The appearance is similar on tryptone, but the formations seem more advanced on proteose peptone and show some wrinkling and radii on an increase in the concentration. There is frosting on all mediums.

With 1 per cent dextrose the growth on 1 per cent peptone is waxy, light gray and smooth except for an occasional speckling of white mycelium. On 4 per cent peptone the growth shows more aerial mycelium, but the mycelium becomes more matted as the concentration of peptone is further increased. On 1 per cent proteose peptone the growth shows the white mycelial duvet, those on the higher concentrations showing mycelial spicules and frosting. On 1 per cent tryptone the growth shows a pleomorphic white mycelium which becomes matted and shows spicules as the concentration of tryptone is increased; the mycelium, even on the 1 per cent concentration, has a fawn tint. The extent of the growth on tryptone is increased over that on the aforementioned mediums. With 4 per cent dextrose the growth on 1 per cent peptone is smooth and waxy, with rare, waxy mycelium heaped radially to the plant; the mycelium becomes matted on 4 per cent peptone and tends to become more profuse with a further increase in the concentration of peptone. There is not as extensive a growth with 4 per cent dextrose as with 1 per cent dextrose. On 1 per cent proteose peptone the growth is white and mycelial, but it becomes waxy with an increase in the concentration. The growths on 1 and 4 per cent tryptone are pleomorphic, and no growth occurs on 8 and 12 per cent tryptone. This is the only instance in which growth does not seem to increase with an increase of the concentration of dextrose and peptone.

*Glenospora Gammeli.*—On 1 per cent peptone there is a layer of white mycelium; as the concentration of peptone is increased, coarser mycelium, spicules and addi-

tional frosting become apparent, together with bits of white mycelium here and there. The growths on proteose peptone and tryptone are similar.

With 1 per cent dextrose the growth on 1 per cent peptone shows a white mycelium, with an area cratered centrally and slightly powdery, through which shows a frosted surface below. The mycelium becomes more matted and spicule-like as the concentration of peptone is increased. On proteose peptone the growth seems further advanced; and on 12 per cent peptone there seems to be a tendency for the spicules to become more sparse and finer than on other concentrations. The growths decrease on 8 and 12 per cent tryptone and become smoother; otherwise they resemble those on peptone.

With 4 per cent dextrose the mycelium is less evident; and the growth is more wrinkled and more uniformly powdered, with frosting at the edge, on 1 per cent peptone with 4 per cent dextrose than with a reduced concentration of dextrose. As the concentration of peptone is increased, the growth shows more aerial mycelium. On 1 per cent proteose peptone the growth is waxy, but it shows aerial mycelium with an increase in the concentration. Tryptone acts as peptone, causing the growth to produce feelers which attach themselves to the glass on the 4 per cent concentration; there is a hardly appreciable growth on 8 and 12 per cent tryptone.

The growth seems to increase with an increase in the concentration of peptone and dextrose, except probably in the case of tryptone. When the mycelium disappears a fawn color is assumed. The growths on 1 per cent peptone and 1 per cent proteose peptone show more cratering and wrinkling than those on the other mediums.

GROUP D

*Endodermophyton Tropicale.*—The growths on 1 per cent concentrations of the peptones seem somewhat powdery; on mediums of higher concentration the growths become wrinkled and heaped up; on 8 and 12 per cent proteose peptone the growths resemble wrinkled cream-puffs, their coarseness increasing with the concentration of the peptone.

With 1 per cent dextrose there is more growth, wrinkling increasing with an increase in the concentration of the peptone. The growth tends to increase on 1 per cent proteose peptone.

With 4 per cent dextrose the growths are darker and slightly more profuse, but on tryptone they decrease with an increase in the concentration, until there is no growth on 12 per cent tryptone.

I have considered the collapsed cream-puff appearance typical for most of these growths.

GROUP F

*Acladium Castellani.*—On 1 per cent peptone there is a small, shell-like growth, with faint radii and a concentric rim; it is fawn-colored and slightly raised. With an increase in the concentration the growths become black; they are finely radiate on the 4 per cent concentration and more coarse on 8 and 12 per cent concentrations; the growths become lighter at the borders as the concentration increases. On 1 per cent proteose peptone the growth is petal-like, being raised at the center, where there is a sparse white mycelium. The growths on all the mediums darken, but on 4 per cent proteose peptone the growth is black, irregularly heaped up and radiate, with a serrated edge while on 8 and 12 per cent proteose peptone the growths are more a fawn color. On 1 per cent tryptone the growth is black, but it becomes lighter as the concentration of tryptone is increased, that on 4

per cent tryptone being black, but those on 8 and 12 per cent tryptone being fawn-colored.

With 1 per cent dextrose the growth increases and is darkened. On 1 per cent peptone the growth is a light fawn color, becoming dark toward the center of the colony, with fairly deep radii; the growth on 4 per cent peptone is the darkest, those on 8 per cent and on 12 per cent peptone being more fawn-colored. With an increase in the concentration of peptone there seems to be a slightly greater increase in wrinkling. On proteose peptone the growth seems to be more waxy and heaped up with an increase in the concentration and is fawn color. On 1 per cent tryptone there are well formed, multiple concentric rings, with radial folds, and the color is dark brown; with an increase in the concentration the rings become less pronounced and a granular appearance develops.

With 4 per cent dextrose the medium is darkened and there is probably an exaggerated growth, with more heaping, wrinkling and mycelial stubble centrally with an increase in the concentration of the peptones.

The growth apparently increases with an increase in the concentration of the peptone and sugar.

*Candida Candida.*—On the peptones with an increase in the concentration the growths become coarse, wet and wrinkled; there is a subsurface mycelium which decreases with an increase in the concentration. On proteose peptone the growth is slightly less than that on peptone but is more heaped up and radiate, and the subsurface mycelium is sparse On tryptone the growth is more profuse than that on peptone; there is less subsurface mycelium and it decreases with an increase in the concentration. There are a few white granules on 8 and 12 per cent proteose peptone and some radii on 12 per cent proteose peptone.

With 1 per cent dextrose the growths are more profuse and latticed on 1 and 4 per cent peptone than on the aforementioned mediums; the growth is wetter on 4 per cent peptone and shows a little fine stubble mycelium; development is radiate from the points of inoculation. There is stubble mycelium on 8 per cent peptone; on 12 per cent the growth is more blotchy. On mediums of more than 4 per cent concentration there seems to be a decrease in subsurface mycelium with an increase in the concentration. On proteose peptone there are more profuse growths than on peptone, and subsurface mycelium decreases with an increase in the concentration. The growth is more moist on tryptone than on the aforementioned mediums, and on 8 and 12 per cent tryptone the growth appears to be sprinkled with coarse particles.

With 4 per cent dextrose the growth on 1 per cent peptone shows a smooth, waxy and radiate growth, with a slightly heaped-up central area; the growth increases as the concentration of peptone is increased and becomes more irregular and heaped; stubble mycelium appears; a narrow edge is radiate, but the rest of the growth is corrugated. The growths on all mediums are moderately wet, and there is less subsurface mycelium with an increase in the concentration of peptone. The growth is much heaped up and irregular on proteose peptone. On 1 per cent tryptone the growth is smoothly radiate from a somewhat granular center; the granular center becomes larger with an increase in the concentration of tryptone until it is the color of brown sandpaper on 12 per cent tryptone. The growth decreases with an increase in the concentration of tryptone.

The subsurface mycelium decreases with an increase in the concentration of peptone and probably with an increase in the concentration of dextrose; the mycelium is least evident on proteose peptone.

*Monilia Albicans.*—On 1 per cent peptone there is little else than subsurface mycelium, which decreases with an increase in the concentration of peptone. On 4 per cent peptone the growth shows radii, on 8 per cent peptone, a latticed center and on 12 per cent peptone a heaped-up and somewhat radiate formation. On proteose peptone the growths are less uniform, wetter and more granular and show very little subsurface mycelium. On 1 per cent tryptone there is more subsurface mycelium; on 4 per cent tryptone the growth becomes more uniform and radiate, with a latticed center. The growths become less latticed, wetter and more granular as the concentration of tryptone is further increased. The growths increase with an increase in the concentration of the peptones.

With 1 per cent dextrose and peptone a latticed center appears which becomes finer and more heaped up as the concentration is increased; the growth is more radiate on 1 per cent peptone, those on the higher concentrations being more latticed and more radiate. On proteose peptone the growths are wetter and not as finely latticed as on the aforementioned mediums; on 4 and 8 per cent proteose peptone the growths give a mucoid effect, and on 1 and 12 per cent proteose peptone, a coarse, latticed effect. On 1 per cent tryptone the growth has a latticed, honeycomb center; the growth on 4 per cent tryptone is more uniformly latticed; the growth on 8 per cent tryptone is more heaped up and the growth on 12 per cent tryptone is more granular.

With 4 per cent dextrose the growth on 1 per cent peptone has a honeycombed center, which is radiate and heaped up; there is less lattice effect on 4 per cent peptone, but the edge of the growth on this concentration and almost all of the 8 per cent peptone, are coarsely granular, with radii at the edge; the growth on 12 per cent peptone is very much latticed throughout. The growth is not uniform on proteose peptone. The growths are coarsely granular on 4 and 8 per cent tryptone, leaflike on 1 per cent tryptone and somewhat liquid on 12 per cent tryptone.

Generally, there is greater growth with an increase in the concentration of peptone and dextrose.

*Sporotrichum Schenckii.*—On 1 per cent peptone there are a powdery surface like whitewash and subsurface mycelium, of which there is less as the concentration of peptone is increased. On 4 per cent peptone there is a purposeless growth, and on 8 and 12 per cent peptone the growths are increasingly more irregularly radiate. On 1 per cent proteose peptone there are a suggestion of radii and a white powdery appearance at the edge of the growth; with the increase in concentration the growth becomes wet and mucoid. On 1 per cent tryptone frostiness and subsurface mycelium appear, which decrease with an increase in the concentration. White granules appear on 8 and 12 per cent tryptone. The extent of the growth increases in this group and with an increase in the concentration there is an increase in radii.

With 1 per cent dextrose the growth on peptone is increased; on 1 per cent peptone the growth is spattered with large grains of powder resembling whitewash and a little subsurface mycelium. The growth on mediums of higher concentration are waxy, with radii and a brushlike mycelium at the periphery. On 1 per cent proteose peptone there appears white powderiness like down, with radii giving the appearance of wrinkled doeskin; there is a scant subsurface mycelium, and isolated colonies give a starlike effect with their radii. On mediums of a higher concentration the growths are more mycoid and wetter. On 1 per cent tryptone the growth is radiate but not powdery; on other concentrations of tryptone the growths are similar to those on peptone.

With 4 per cent dextrose the growth on 1 per cent peptone is lattice-like and radiate, with a smooth formation on the surface at the periphery. On 4 per cent peptone the growth is like a shield spattered with coarse sand (mycelial stubble); on 8 per cent peptone the growth becomes irregularly radiate and heaped up. On 12 and 8 per cent peptone the growth increases and is wetter. On 1 per cent proteose peptone the mycelium is sparse like sprigs and there is a waxy granular appearance; on higher concentrations the growths become wetter. On 1 per cent tryptone there is a dry granular growth; on 4 per cent tryptone the growth is finely radiate, and on an increase in concentration the growths are coarsely granular, with nests of radii.

An increase in the concentration of sugar and peptone results in an increased growth.

GROUP G

*Geotrichum Bachmann.*—On peptone the growth increases with an increase in the concentration. There are slightly more extensive growths on proteose peptone and tryptone than on peptone. On 12 per cent tryptone there are white granules.

With 1 per cent dextrose the growth increases, becoming more blotchy. The growths are blotchy on the proteose peptone; that on 1 per cent proteose peptone is smoother and more radiate. On 1 per cent tryptone there is a tendency to heaping, with radii; on other concentrations granules are noted.

With 4 per cent dextrose the growth on 1 per cent peptone is smooth, with a suggestion of a concentric ring; the rest is blotchy but is increased in thickness over the growth on 1 per cent dextrose. On proteose peptone the growths are smoother but have an irregular surface. On 1 per cent tryptone the growth is more frosted and puckery; on 4 per cent tryptone there is an irregular ribbed appearance, with a scant, white fuzz over the surface; on 8 and 12 per cent tryptone granules are noted.

*Lichtheimia sp.*—As the concentration of peptone increases, the aerial growths become successively diminished, until on 8 and 12 per cent peptone a frosted, waxy surface with a border showing scant low mycelia appears. On 4 per cent peptone mycelium is much reduced, low and matted to the surface. The growths on proteose peptone are similar, but a reaction to an increase in the concentration of peptone occurs sooner, and the growths are thicker and become granular. On tryptone the growths are similar to those on peptone, but changes begin on a slightly lower concentration.

With 1 per cent dextrose there is more mycelium and the growth is more extensive; on 4, 8 and 12 per cent peptone, successively, the mycelium fills less of the tube and the growths become frosted. This occurs on tryptone and proteose peptone.

With 4 per cent dextrose the mycelium becomes more profuse and fills less of the diameter; on 8 and 12 per cent peptone the growths are more drawn. On 8 and 12 per cent proteose peptone the growths are like beeswax. Aerial mycelium is noted in all the tubes of tryptone.

Aerial mycelium increases with an increase in the concentration of dextrose and decreases with an increase in the concentration of peptone, but the effect of peptone is largely offset when 4 per cent dextrose is used with peptone and tryptone.

*Oospora Humi.*—There is a low, short, velvety mycelium on peptone; on 12 per cent peptone there are fewer than on the other concentrations; otherwise the surface is frosted and the growth increases with an increase in the concentration of peptone. The growths on proteose peptone are similar to those on peptone but

with less mycelium. On tryptone of more than 1 per cent concentration the growths have a ribbed and granular appearance; and white mycelium is largely absent from the growths on 4 and 12 per cent tryptone. The growths are more profuse on tryptone than those on peptone.

With 1 per cent dextrose the growths are more extensive, of somewhat ribbed appearance. On 1 per cent proteose peptone the growth is more profuse and ribbed radially. Growths on tryptone are more blotchy.

With 4 per cent dextrose the growth on 1 per cent peptone develop a white mycelial layer, giving a powdery appearance; with an increase in the concentration the growths become thicker and more like beeswax, with an appearance of sandpaper on 12 per cent peptone. The growths are more profuse on proteose peptone and tryptone than on peptone.

*Scopulariopsis Brevicaulis.*—As the concentration of peptone is increased the growths become more wrinkled, lighter brown, wetter and more finely granular and there is an increase in aerial mycelium. There is a tint of green on 12 per cent peptone. There is more interlocked wrinkling on proteose peptone, with more growth, more wrinkling and more uniformity of appearance. On tryptone the growths are more wrinkled than those on peptone, and on 8 and 12 per cent tryptone the growth is almost entirely wet.

With 1 per cent dextrose the growth on peptone shows less wetting; the color is not lost as quickly with an increase in the concentration of the peptone, but heaping up and a tendency to radii are more marked, and there is probably slightly more aerial mycelium. On proteose peptone the growth is wrinkled at the center, with white granules on the 1 per cent concentration. On 1 per cent tryptone there is a verrucoid appearance at the center; on 8 and 12 per cent tryptone the growths are partly wet. The mycelium is matted at the center of the growth on 8 per cent tryptone, and fine, long, hairlike ends of mycelium are seen at the center of the growth on 12 per cent tryptone.

With 4 per cent dextrose the color on 1 per cent peptone is diminished; more wetting is noted on 8 per cent peptone, and there are areas of white mycelium. The growths become lighter as the concentration of peptone is increased. The growths are much wrinkled on proteose peptone and become lighter in color as the concentration of peptone is increased. On 1 per cent tryptone the growth shows a verrucoid appearance and is cream-color; it is heaped up and somewhat concentric and has a scattering of fine white powder. The growth on 4 per cent tryptone is fine, like verruca, with a brown powdery surface; the growths on 8 and 12 per cent tryptone are wet and very wrinkled, with practically no mycelia, and are a lighter brown than that on 4 per cent tryptone.

The growths seem to increase with an increase in the concentration of peptone and sugar.

*Willia Anomala.*—On peptone the growths increase with the increase in the concentration. The edge is irregularly serrated on 1 per cent peptone; the growths seem lumpy on mediums in higher concentrations. The colonies are more blotchy on proteose peptone and the growths are more profuse than those on peptone. On tryptone the growths are similar to those on peptone.

With 1 per cent dextrose the growths increase with an increase in the concentration of the peptones, especially of proteose peptone.

With 4 per cent dextrose, the growth on 1 per cent peptone shows radiate surface mycelium at the border and into the medium (the development of mycelium is slight on 1 per cent peptone with 1 per cent dextrose); the growth is more pro-

fuse than that with 1 per cent dextrose. The growths on proteose peptone are smeary. On tryptone the growths resemble those on peptone but are drier, with a sandpapery, slightly fuzzy surface and a suggestion of radii.

## GENERAL OBSERVATIONS

In a perusal of the literature I have found little reference to the use of tryptone and proteose peptone for the growth of pathogenic fungi. Leonian [2] used proteose peptone to a limited extent. Because of the specialized use of tryptone and proteose peptone in the cultivation of micro-organisms and because of their variation in composition,[3] it seemed fitting to use them in the effort to find a better medium for the cultivation of pathogenic fungi. The mediums were prepared in the same way as those of peptone used in the series reported previously,[1] and the organisms were grown under similar conditions.

The results on the several mediums differed in numerous respects. In general, with like concentrations of the three peptones there seemed to be more advanced changes on proteose peptone and least advanced changes on tryptone. Often with 8 and 12 per cent proteose peptone and 4 per cent dextrose and with 12 per cent proteose peptone and 1 per cent dextrose solidification with 1.5 per cent agar did not take place, in which case the tubes were discarded. With 4 per cent dextrose and 8 and 12 per cent tryptone, diminished or no growth occurred in several instances, indicating a factor interfering with the growth of the organisms.

A change most frequently noted on proteose peptone and less often noted on tryptone was iridescence of the surface of the medium about the plant. Since this occurred frequently, I believe that it was probably not sufficiently characteristic or fundamental to be of value in differentiation.

In general, on all mediums the growths increased with an increase in the concentration of the peptones and dextrose. In most instances pleomorphism increased with an increase in the concentration of dextrose but decreased with an increase in the concentration of peptones.

There were a few instances in which a constant percentage of dextrose and an increase in the concentration of peptone seemed to result in increased pleomorphism. It is possible that the ratio of these two ingredients was determinant. With an increase in the concentration of peptone there was an increase in wrinkling, cratering, wetness, frosting, waxiness and coarseness of the mycelium (stubble mycelium, etc.), especially on mediums in which dextrose was present. There

2. Leonian, L. H.: Effect of Position of Inoculum on Growth of Some Trichophytons in the Presence of Dyes, Arch. Dermat. & Syph. **25**:1016 (June) 1932.

3. Manual of Dehydrated Culture Media and Reagents, ed. 4, Detroit, Difco Laboratories, 1933.

were some indications that waxiness occurred in the stage following wetness of the mycelium on an increase in the concentration of peptone. In a few growths subsurface mycelium was marked; this was present especially in the growths on 1 per cent peptone and decreased with an increase in the concentration of peptone.

In general the growth on the several peptones was somewhat similar. I have not attempted to list in detail the variations in color, for, as stated previously, this would be difficult because of changes in color resulting in many of the mediums from an increase in the concentration. An attempt has been made in the accompanying table

*The Differentiation of Various Organisms According to the Medium Employed*

| | Peptone | | Proteose Peptone | | Tryptone | |
|---|---|---|---|---|---|---|
| | M* | D | M | D | M | D |
| Achorion Schoenleinii | R, W1, L1<br>W4 | 2½<br>3 | R, S1, W1 | 3 | R, W1<br>S1 | 3<br>3½ |
| Epidermophyton cruris | L, W1, L1 | 3 | WP, W1, LT1<br>WP1, LP | 3<br>3½ | LT, LT1 | 3 |
| Epidermophyton inguinale | R, W4,<br>W1, S4 | 1½<br>2 | WP<br>LP | 2<br>2½ | WT1, RT1<br>LT1 | 1½<br>1½ |
| Indiella americana | S1<br>S4 | 2½<br>3½ | SP4 | 2½ | ST1 | 2½ |
| Microsporon Audouini | L1<br>W1 | 3<br>2 | WP1 | 2 | WT, ST1<br>WT1, LT1 | 2<br>2 |
| Microsporon felineum | R, L1, R4<br>W1, S1 | 1<br>1½ | L, R, L1<br>R1 | 1<br>1½ | LT<br>R, L, L1 | 2<br>1 |
| Microsporon gypseum | L1<br>W1 | 2½<br>3½ | LP1<br>WP1 | 4<br>3 | LT1<br>WT1 | 3½<br>3 |
| Trichophyton crateriforme | L<br>W1, L1 | 3<br>2½ | LP<br>SP1 | 3<br>3½ | RT<br>ST1 | 2½<br>3½ |
| Trichophyton granulosum | R | 2 | RP | 1½ | RT, RT1 | 2½ |
| Trichophyton gypseum-asteroides | R, R1 | 1½ | WP1<br>LP1 | 2½<br>3 | RP, WT<br>LT1 | 2½<br>2½ |
| Trichophyton gypseum-lacticolor | W1<br>R, R1 | ½<br>2½ | LP, WP<br>LP1, RP1<br>WP4, LP4 | 2<br>2½<br>2½ | WT, LT1<br>LT, WT1 | 2½<br>2 |
| Trichophyton interdigitale | R, R1, R4<br>L1 | 1½<br>1½ | RP1, RP4 | 1½ | RT1, RT4 | 1½ |
| Trichophyton niveum | L, W1 | 2½ | LP, WP1 | 2½ | RT,<br>LT, WT1 | 3½<br>2½ |
| Trichophyton sulfureum | S4<br>W4 | 2½<br>3 | RP, SP1 | 2 | RT1 | 2 |

* Under M is indicated the medium and under D the differentiation.

to indicate mediums giving good differentiation. The judgment as to differentiation may be questioned. The suggestions with reference to increasing the differentiation are along the line of reducing aerial mycelium. For such a reduction, with some organisms a high concentration of peptone was necessary. In fact, variation with regard to the reduction of aerial mycelium by means of an increase in the concentration of peptone occurred to a considerable degree with different organisms. To determine whether this method is entirely feasible will necessitate further study.

The differentiations given in the table are only comparative and show the instances in which higher concentrations and variable concentrations were necessary for the best differentiation. The observations emphasize the fact that it is not always with peptone that the best morphologic pictures are obtained. If the average differentiation is estimated from the higher differentiation values for the several peptones the value for peptone and proteose peptone is 2.54 and for tryptone 2.57. These values are practically equal, demonstrating that there is comparatively little difference in the value of these peptones. However, one factor is not considered, and that is pigment. The pigment of proteose peptone is often imparted to the growth, interfering with recognition of the inherent pigment of the organism. Sometimes the growth on proteose peptone is in excess of that desired, or the medium fails to liquefy properly. On the other hand, tryptone is a light-colored medium, which is of considerable value since it can easily be substituted for peptone. In fact, its clarity often makes it superior to peptone.

### THE PHYSICAL CHEMICAL CHARACTERISTICS OF THE MEDIUM

The importance of physical chemical characteristics of the medium has been mentioned previously. These characteristics are surface tension, osmotic pressure and viscosity.

Surface tension is decreased on an increase in the concentration of peptones up to a certain point. It is possible that this property of peptones of decreasing surface tension is a reason for their serving so efficaciously in the nourishment of organisms. One needs only to recall the necessity of the reduction of surface tension either by the type of food one eats or by bile from the gallbladder in order to get proper digestion and assimilation of food in the duodenum. This reduction of surface tension, according to Gibbs' principle, would be most marked at the medium-organism interface, where the assimilation of nutriment takes place. This reduction would be interfered with by an excess of adsorbing interfaces of nonliving nature. Such adsorbing surfaces might be provided by carbonization in the autoclave. Naturally this feature would be variable and might influence not only the nutrient quality of the medium but also the availability of the nutriment.

Osmotic pressure is important not alone with reference to the medium but also with reference to the organisms. In plants this varies considerably. For example, it is much greater in desert plants.[4] This is only natural, since the elevation of pressure as a result of a decrease in vapor pressure would decrease transpiration and prevent the plant

4. Fitting, Hans: Ztschr. f. Bot. **3**:209, 1911. Livingston, B. E.: Plant World **14**:153, 1911.

from drying. Green plants, however, are not identical with fungi, since in fungi there are neither arteries for the transport of nourishment nor cell spaces but merely a unity by individual cells. Therefore, these individual cells are the factors in maintaining suitable osmotic pressure. It has been observed that Aspergillus niger and Penicillium may develop an osmotic pressure as great as 157 atmospheres when grown in concentrated dextrose or saline solutions.[5] Thus, several factors may play a part in the maintenance of sufficient osmotic pressure, with normal turgidity and function of the cell, the vapor pressure resulting from humidity and temperature, the movement of air and the relative osmotic pressure of the nutriment. Aspergillus niger and Penicillium are comparatively more hardy than many of the pathogenic fungi and can meet the demanded variation probably more efficiently and without as much change as occurs in the latter organisms. In addition, they do not show the variation in the morphology of the colony shown by many pathogenic fungi, which could well be influenced by the changes already mentioned.

In order to test the effect of osmotic pressure on pathogenic fungi I planted organisms on W mediums containing the following concentrations of chemically pure sodium chloride: 0.1, 0.5, 1 and 1.5 per cent.[6] While the morphology was altered slightly in certain instances by increasing the osmotic pressure in this manner, the striking similarity of the colonies was not destroyed.

Another factor not mentioned previously is viscosity. In this work I have treated the physical chemical factors as though dealing with a liquid medium, when, in fact, I was employing a medium in which agar was used for solidification. Because of the ready diffusibility of the liquid medium through the agar, this treatment was justifiable, since the units utilized by the organism were liquid and of the composition and ingredients, except for the agar, of the liquid medium. Viscosity probably determines to some extent the availability of this liquid portion, since by an increase in viscosity there is an increase in the friction between the layers of fluids and less ease of their movements and diffusion. This viscosity in mediums of higher concentrations apparently makes solidification by 1.5 per cent agar impossible. My work on this subject has not shown sufficient results to be reported.

With reference to surface tension, peptone mediums with dextrose have shown considerable variation.[6] The most significant observation has been that the surface tension of peptone mediums containing 1 per

5. Atkins, W. R. G.: Some Recent Researches in Plant Physiology, London, Whittaker & Co., 1916, p. 328.

6. Williams, J. W.: Physical Chemistry and the Growth of Certain Pathogenic Fungi, to be published.

7-11. Footnotes deleted by author.

cent dextrose is lower than that of mediums containing 4 per cent dextrose. My observations also indicate that when the ratio is maintained there is a significant correspondence of surface tension over a considerable range. The observations on surface tension also seem to check with the morphologic appearances. When the surface tension is lower, there is in the majority of instances a tendency to less aerial mycelium and less pleomorphism. Since W1 medium has a much lower surface tension than Sabouraud's proof medium one cannot ignore this variation. The advantage of greater concentration (possibly not beyond 8 per cent) of peptone when sugar is used may possibly be explained, at least in part, by this physical chemical characteristic. In most instances also an increase in sugar seems to increase both the surface tension and the pleomorphism. Of course, there is a coincident increase in the osmotic pressure, which I do not think has been completely ruled out. It is logical to assume that an increase in the surface tension would tend to push mycelium to greater lengths. With reference to subsurface mycelium, however, the explanation is not so tangible. As yet I do not think that I have a significant clue to its cause.

When the surface tension of Sabouraud's medium (S4) is lowered by means of sodium taurocholate,[6] there is in many instances a tendency to frosting and development of coarse mycelium, similar to that on such mediums as W1, in which the ratio of peptone to dextrose is increased. These appearances seem better demonstrated with mediums with a surface tension of 52.5 dynes (28 C.) or lower, since when one-half the concentration of W medium is used, with a resultant increase of surface tension of several points, the marked effects are not noted and the mycelium seems more aerial and less compact.[6] Also, when the osmotic pressure of W medium is raised to 18.69 atmospheres (25 C.) with sodium chloride,[6] there is an increase in wetness and in some instances an increase in the area of frosting. At this osmotic pressure, however, no marked change was noted in the mycelium.

It will be necessary to use additional substances for lowering the surface tension and additional salts for increasing the osmotic pressure before any definite conclusions can be drawn with regard to the exact effects of surface tension and osmotic pressure. I am becoming increasingly aware of their importance in the morphology of the colonies of pathogenic fungi when peptones or amino-acids and dextrose are used. In bacteriology [6] I think that they are equally important, although there has been a tendency to forget them. A device for the measurement of surface tension, preferably an interfacial tensiometer, and a method for determining osmotic pressure, preferably by a study of the relative effect of the constituents of mediums and a substance of known molecu-

lar weight, such as sodium chloride, on cells,[6] should be standard in every bacteriologic and mycologic research laboratory. In the latter test, if red blood cells are used one must realize that some constituents of the medium may have a hemolytic effect (but possibly due to surface tension) and that this effect may not be applicable to pathogenic fungi. Such an effect may be noted with certain salts, such as sodium taurocholate.[12]

## COMMENT

In this paper I have attempted to emphasize the morphologic characteristics of certain pathogenic fungi. I think that this is justifiable, since there has been considerable recent emphasis on the microscopic characteristics of these organisms with reference to classification both from the point of view of methods of classification [13] and from the point of view of practical identification by the laboratory worker.[14] Another justification is the tardy appreciation of the importance of rough and smooth colonies of bacteria. Scientists seem to have been so enamored of the microscope and the microscopic picture that for many years they neglected what they could see with their eyes. I think that it is better to see first what one can with the naked eye and then, when completely satisfied with those observations, to resort to the microscope.

I have also emphasized the physical chemical properties of the mediums studied. I feel that this should be a function of every study of this nature. Not only this but also the fundamental chemical character of these organisms is important. The latter feature is being investigated by Dr. B. S. Gould, of my department, and will be reported later when a sufficient number of results are accumulated.

It is needless to say that variations of many of the colonies studied are very confusing. For example, Trichophyton granulosum grown on Sabouraud's proof medium showed a pleomorphic white growth. When transplanted to W1 medium the growth lost this pleomorphism, became radiate, with a covering like doeskin, and had a central area of dull raspberry. The question arises: Which is to be considered typical? It seems that the answer should be the growth on W1 medium. This stable morphologic picture for W1 medium does not always occur with

12. Williams, J. W.: Proc. Soc. Exper. Biol. & Med. **27**:913, 1930; **28**:741, 1931.

13. Ota, M., and Langeron, M.: Ann. de parasitol. **1**:305, 1923. Vuillemin, P.: Compt. rend. Acad. d. sc. **180**:102, 1925. Guiart, J., and Grigorakis, L.: Lyon méd. **141**:369, 1928. Grigorakis, L.: Ann. de dermat. et syph. **10**:18, 1929. Emmons, C. W.: Dermatophytes: Natural Grouping Based on the Form of the Spores and Accessory Organs, Arch. Dermat. & Syph. **30**:337 (Sept.) 1934.

14. Shaw, F. W.: J. Lab. & Clin. Med. **20**:113, 1934.

the first transplant. It appears that the morphologically variable organisms must reach their stride for the particular medium, and if stability is to be reached the medium must be one of stabilizing character on which the organism shows no variation or easily recognizable morphologic variations. Thus, the character of an organism may vacillate from transplant to transplant from one easily recognizable type of colony to another.

I have had the opinion that a medium of a ratio of constituents fairly near that of the skin might be desirable, and in W medium the tendency is in that direction. It is probable that horn, skin or hair might be better, but technical difficulties are encountered. I am having digests made of hair, and I am growing organisms on horn, hoof and skin in an effort to assess their merit.

Some of the pathogenic fungi have been looked on by many workers with too much awe. For example, speaking from experience with W1 medium, it seems that $p_H$ has been overemphasized. Apparently a considerable variation of osmotic pressure is allowable, and certainly plenty of concentration of the medium is permissible as long as the same ratio is maintained.

Amino-acids as substitutes for peptone may be pure, but they are expensive and at present are limited largely to research work. There is some indication that ratio and surface tension may act the same, at least in some amino-acids, as they do in peptone. Apparently some organisms do not relish certain amino-acids; at least, their application to the cultivation of organisms is not as wide as that of peptones. This limits their use, except when time and expense are minor items. Therefore, why not adapt peptones, if this is possible, for practical every-day use and reserve consideration of the amino-acids for special occasions? This also applies to synthetic mediums in which amino-acids are not ingredients.

## SUMMARY

The variation of the morphology of the colony with a change of the ratio of dextrose to peptone, proteose peptone or tryptone with reference to physical chemical characteristics has been discussed.

The advantages of mediums of a ratio different from that of Sabouraud's proof medium were cited. A medium of 4 per cent peptone, 1 per cent dextrose and 1.5 per cent agar, with a $p_H$ which may vary from 5.2 to 8, is considered of great value.

Methods of estimating the differentiation of colonies were suggested.

Morphologic stabilizing effects of mediums were discussed.

An attempt was made to divide the organisms according to the morphology and the production of pigment.

A correlation of surface tension, osmotic pressure and morphology of the colony was drawn. The possibility of variation of the morphology on variation of the asparagine-dextrose ratio was advanced as a result of preliminary work. Here, too, a variation of the surface tension similar to that seen when the peptone-dextrose ratio is changed was noted.

The importance of a standard device for estimating surface tension and a standard method for measuring osmotic pressure in every research, bacteriologic and mycologic laboratory was emphasized.

References were given which will serve as a key to the literature.

# HISTOPATHOGENESIS OF PSORIASIS AND ITS ABERRANT LESIONS

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Psoriasis has been accepted as a clinical and histologic entity. The identity of the condition has been conceded. Yet in carefully investigated cases of psoriasis the involvement has eventuated in other conditions, mycosis fungoides, for instance. At times it is difficult, even impossible, to differentiate clinically between psoriasis and certain other scaling dermatoses, such as eczema, the prefungoid stage of mycosis fungoides, syphilis, lupus erythematosus, generalized superficial epitheliomatosis cutis, lichen planus, pyoderma and other conditions. Not infrequently it is equally difficult or impossible to make an unequivocal diagnosis in the laboratory. In many cases of typical psoriasis there are individual lesions that alone do not suggest psoriasis. The object of this investigation is a clinical and microscopic study of borderline cases of psoriasis, atypical psoriatic lesions, eruptions in patients with typical psoriasis and uncommon and rare examples of the disease in an attempt to confirm or refute the identity of the disease and to broaden or narrow the conception of it as a clinical and histologic entity.

The history of the study of the pathology of the cutaneous organ is of great interest and has a direct bearing on the subject matter of this paper; therefore, we shall attempt to sum up briefly the essential facts available.

The Greek physicians of the Attic period brought forth the hypothesis that the fluids of the body were responsible for all dermatoses. This influence limited dermatologic knowledge until leprosy was definitely found to be controlled only by isolation. Opinions change slowly, and it was only with the help of an epidemic of syphilis which swept from country to country that an outside causative factor was considered for the dermatoses. In the early part of 1700 physicians

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began in a crude way to formulate classifications and recognize many of the dermatoses as they are known today.

It remained for Willan [1] (1798) to classify the dermatoses seriously. He did this purely from a morphologic standpoint, placing in a few main groups multiple entities with polyvalent etiology. The classification was suitable for that period but was gradually outmoded owing to constantly increasing knowledge. Entity after entity was removed, leaving an almost unrecognizable skeleton.

Von Hebra [2] was responsible for two great advances in dermatology. First, he was instrumental in causing the skin to be considered as an organ of the body capable of having its own functions and diseases, and, second, he was credited, in conjunction with Rokitansky,[3] with having fathered cutaneous pathology. They were followed by Virchow,[4] Unna,[5] to whom is due so much credit in the advancement and dissemination of histopathologic knowledge, published his detailed work in 1894. Munro [6] (1893-1898) added to the histopathology of psoriasis by describing the Munro-Sabouraud micro-abscesses and explaining their formation. Haslund [7] (1912) reviewed the literature and described 9 cases of psoriasis in detail. He gave the views of various contemporary workers whose opinions concerning the histopathogenesis of the psoriatic lesion were at great variance. Civatte [8] (1924) gave an excellent differ-

1. Willan, R.: On Cutaneous Diseases, Philadelphia, Kimber & Conrad, 1809; Die Hautkrankheiten und ihre Behandlung systematisch beschrieben. Aus dem Englischen übersetzt, und mit einigen Anmerkungen und einem Anhange begleitet von Friedrich Gotthelf Friese, Breslau, J. F. Korn, 1799-1806; Delineations of Cutaneous Diseases, edited by Thomas Bateman, London, Longman, Hurst, Rees & Company, 1817.

2. von Hebra, H.: Morbid Changes of the Skin and of Its Appendices with Their Relations to Diseases of the General Organism, translated from the German by M. Hirschfeld and A. Feinberg, St. Petersburg, Ettinger, 1885.

3. Rokitansky, C.: Handbook of General Pathological Anatomy, Vienna, Braumuller & Seidel, 1842-1846.

4. Virchow, R. L. K.: Cellular Pathology as Based upon Physiological and Pathological Histology, translated from the second edition by Frank Chance, New York, R. M. DeWitt, 1860.

5. Unna, P. G.: The Histopathology of the Diseases of the Skin, translated from the German by Norman Walker with the author's assistance, New York, Macmillan & Co., 1896.

6. Munro, W. J.: Note sur l'histo-pathologie du psoriasis, Ann. de dermat. et syph. **9**:961, 1898.

7. Haslund, P.: Die Histologie und Pathogenese der Psoriasis, Arch. f. Dermat. u. Syph. **114**:427 and 745, 1912.

8. Civatte, A.: Psoriasis and Seborrhoeic Eczema: Pathology, Anatomy and Diagnostic Histology of the Dermatoses, Proc. Roy. Soc. Med. (Sect. Dermat.) **18**:1, 1924.

entiation of psoriasis and seborrheic eczema from a histologic point of view. Barber [9] (1930) did much to clear up the status of the pustular lesions in psoriasis.

The era of dermatologic influence is widening. Allergy, physiology, chemistry, histopathology and endocrinology are essential in the evaluation of the dermatoses and their causation.

In this work we studied the histopathologic changes in an attempt to determine the histopathogenesis of psoriasis and its related conditions, well realizing that few cutaneous lesions present typically pathognomonic diagnostic critera; but if reports of other authors are to be relied on psoriasis is one condition which does have a fairly characteristic picture. Therefore, we have taken typical psoriatic lesions on the one hand and aberrant lesions of patients with psoriasis on the other in an attempt to establish:

1. A basic histopathologic formula for typical psoriasis.
2. The relationship of the aberrant lesions to the typical formula.
3. The frequency of aberrant lesions.
4. The status of psoriasis among the inflammatory dermatoses.

In order to make a diagnosis of psoriasis, one should follow a routine system of examination beginning with the scalp, mucous membranes, elbows, knees, genitals, extremities and trunk. The following features should be evaluated in making the diagnosis:

1. *Tache de bougie* (white silvery powder).
2. *Rosii sanglante* of Auspitz (bleeding points).
3. Sites of predilection.
4. Symmetry.
5. Lesions on the extensor or flexor surfaces.
6. Type of scaling.
7. Amount of infiltration.
8. Duration and history of previous attacks.
9. Familial history of psoriasis.

The basis of a study of aberrant lesions would of necessity rest on a similar study of typical lesions, which preferably should be from the same patients but would be of equal value if from patients with no atypical lesions. Therefore, we have studied 150 cases of psoriasis histologically. In 50 of these cases histologic sections were taken from undeniably typical psoriatic lesions and from typical psoriatic sites. Each

9. Barber, H. W.: Acrodermatitis Continua Vel Perstans (Dermatitis Repens) and Psoriasis Pustulosa, Brit. J. Dermat. **42**:500 (Nov.) 1930; Pustular Psoriasis of Extremities, Proc. Roy. Soc. Med. (Sect. Dermat.) **26**:329 (Feb.) 1933.

case was passed on by three qualified dermatologists before a specimen was taken for section. With these sections forming a basic structure or formula, we were able to compare the aberrant lesions of 100 patients with those of patients with typical lesions and from these draw our conclusions.

In the basic histopathologic formula for typical psoriasis we have found the following essential points in the relative rate of occurrence. Charts were kept to note every change from normal, and therefore each item will be referred to on a percentage basis. Beginning at the outermost layer we found that the silvery laminated scales were composed for the most part of hyperkeratosis and, to a much less degree, of parakeratosis, which tended to be patchy and alternated with the granular layer. We found a dry, irregular, moderately thickened epidermis. The epidermis is referred to as dry, although the intercellular lymph spaces of the rete Malpighii were widened and moderate exocytosis and exoserosis were constantly in progress. The prickle cells appeared pale and sometimes swollen; often the degeneration progressed until the nuclei became flattened or crescentic and migrated to the edge of the cell, constituting hydropic degeneration. These cells were shed as the underlying epidermal cells proliferated. The complete absence of keratohyalin, with the formation of an imperfectly keratinized granular layer, was not a conspicuous feature. The parakeratosis alternated with the granular layer in 44 per cent of the cases and was sparse, that is, in small areas, in 30 per cent. The so-called Munro-Sabouraud abscesses, which are composed of broken-down cellular elements, were present in 36 per cent of the cases studied. A loose interpretation was placed on these abscesses, including grouped cellular detritus in the lamellae of the horny layer as well as similar collections lying between the outer corneous layer and the upper layer of prickle cells; in 24 per cent of the cases these were just below the horny layer and in 12 per cent, in the horny layer. We found the granular layer well developed in 24 per cent of the cases, intermittent in 44 per cent and absent in 12 per cent. Spongiosis was absent in all sections, but in 2 sections small vesicles were found. The basal layer was present and disorganized over a few papillary bodies in 56 per cent.

The rete pegs were irregularly acanthotic and elongated and tended to be polymorphic, some thin, some thick and others fused, and in 16 per cent of the sections the papillae appeared to be particularly tortuous. We believe that this observation was a feature of acanthosis and not the result of an oblique cut of the section, as some of the sections with tortuous papillae were cut on many different angles, yet the same picture was obtained.

The papillary bodies presented moderate edema in 52 per cent of the sections and marked edema in 24 per cent. These bodies tended to be irregular in size and club-shaped. There was moderately severe dilatation of the vessels of the papillary bodies, with sparse round cell infiltration.

The upper layer of the cutis was involved in the edematous process in 100 per cent of the sections, the involvement extending down to the middle layer of the cutis. Interstitial edema predominated over parenchymatous edema. The collagen bundles were swollen in a majority of the sections and dissociated in a few. The lymph spaces tended to show moderate dilatation in 32 per cent of the sections and marked dilatation in 52 per cent, the vessels being dilated accordingly. The walls of the vessels were normal in 90 per cent of the sections. The infiltration of the upper layer of the cutis was focal in 92 per cent and diffuse in 28 per cent.

The adnexa was unaffected. The fat was normal in 98 per cent of the sections, fatty infiltration being present in 2 per cent.

### RELATIONSHIP OF THE ABERRANT LESIONS TO THE TYPICAL FORMULA

Psoriasis is a well defined dermatosis, but in about 1 of 6 cases there are eruptions less monomorphic in clinical type and distribution which confuse the picture. They frequently occupy the sites which psoriatic lesions tend to avoid. The elementary lesions are either of brighter or of duller erythematous tone. The lesions may be exudative or dry, smooth with no scaling or covered with fine micaceous scales or heavy coarse crusts, impregnated with oily substance or devoid of the oily factor but all with the erythematosquamous element. Some lesions clinically resemble psoriasis closely, others little or not at all. We observed lesions ranging in appearance from that of eczema madidans to the fine white scaling of pityriasis alba. It is self-evident that there must be some relation between the various types of aberrant lesions and the typical lesions of psoriasis which each patient presented.

1. *Lesions of an Eczematous Type.*—These lesions were present in a group of 26 cases, or one-fourth the number studied. We placed in this group the cases in which indefinite lesions were present for which no other diagnosis could be entertained. The lesions were of the dry and weeping, erythematous, infectious, crusted and scaling types, none of which, if taken alone, would have been diagnosed psoriasis. We found that in this group the lesions definitely had a different histologic picture in many respects. The epidermis was moist in 32 per cent of the lesions in these cases, against 2 per cent of the cases of psoriasis. The thickness of the suprapapillary layer tended to be normal. Para-

keratosis was patchy or sparse. The granular layer was better developed (40 per cent). Acanthosis was somewhat more general. Spongiosis was noted in 28 per cent of the sections against none in those of psoriasis. Vesicles were found in 24 per cent of the sections. The papillary bodies and the subcutis showed less edema, and the vessels did not show the marked dilatation so generally found in the formula for psoriasis. The difference lay mainly in the epidermis.

2. *Lesions Resembling Seborrhea.*—These were noted in 16 cases. The lesions were taken for the most part from the axillae, chest and scalp and presented yellowish, greasy, branny scales on an erythematous, maculopapular base.

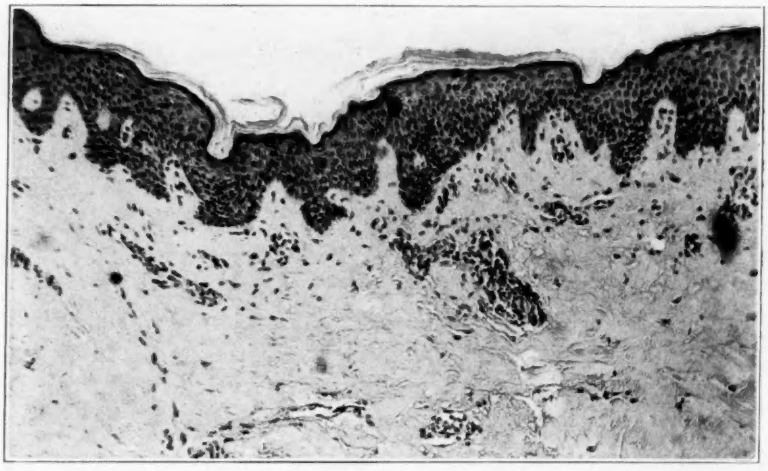

Fig. 1.—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis with no epidermal changes (simple dermatitis).

The question always arises when one discusses psoriasis and seborrhea as to whether the conditions are distinct clinical entities which closely simulate each other, coexisting in the same soil with some lesions clinically indistinguishable, whether one is the stepping-stone or precursor of the other or whether they are phases of the same disease, one being in an intermediate stage at the time of clinical observation. The same may be said concerning all other types of aberrant lesions.

We found that the lesions which closely resembled seborrhea had a pathologic picture that fits in midway between the formula for typical psoriasis and the picture in our 26 cases of the eczematous type. The main characteristics were spongiosis with the formation of vesicles in 20 per cent of the sections, the striking similarity in amount and type of parakeratosis and, in general, the lessened edema of the upper portion of the cutis and the papillary bodies. The change appears to be more

confined to the epiderm than that seen in psoriasis. The grouped subcorneal collection of cellular elements was present in 20 per cent of the sections.

3. *Lesions Resembling Circumscribed Neurodermatitis (Lichen Chronicus Simplex).*—Ten cases were studied. The clinical picture in this group was that of an erythematous, infiltrated, thickened, lichenified, slightly scaly patch, often with smaller corymbiform lesions about the edge of the main plaque. This type of lesion was common over the sacrum just above the intergluteal fold.

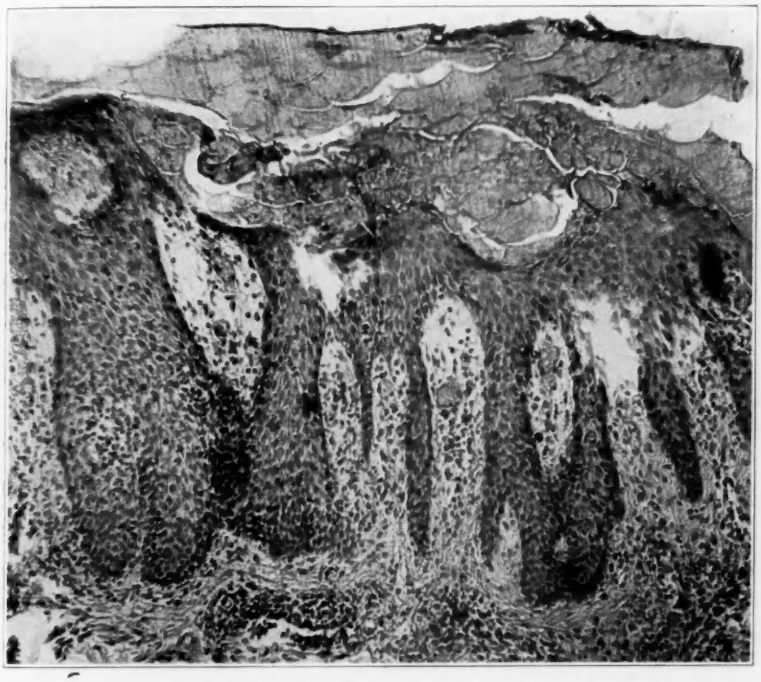

Fig. 2.—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis with eczema-like changes in the epidermis.

Histologically the lesions were predominantly dry with an increased granular layer. Acanthosis was more general than in the cases of psoriasis, and the edema of the papillary and subpapillary area was less. One section showed slight spongiosis and formation of vesicles, which was a long-standing chronic process. Numerous Monro abscesses were noted in 2 of our 10 cases. The lesions differed from those of psoriasis mainly by the thick granular layer.

4. *Pustular Psoriasis.*—Nine cases were studied. Before the discussion of the changes noted in the sections, brief mention will be made of the history of the condition as an entity.

Fig. 3.—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type simulating neurodermatitis.

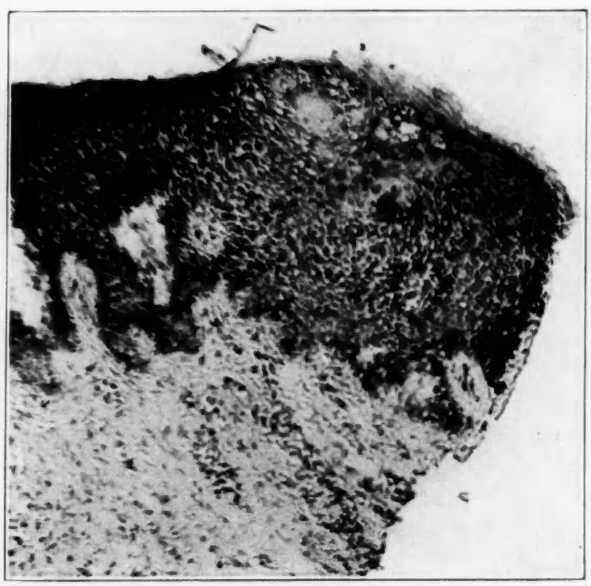

Fig. 4.—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type plus occasional vesicles simulating seborrheic dermatitis.

Strandberg [10] was the first to suggest that pustular lesions might be a feature of psoriasis. Barber [9] in 1930 gave an excellent discussion of this subject, reporting 4 cases, 2 of which were classed as instances of acrodermatitis perstans and 2 as cases of pustular psoriasis. Regarding the former, he favored using the terminology of Dore,[11] "acrodermatitis perstans," rather than "acrodermatitis suppurativa continua" of Hallopeau [12] or "dermatitis repens" of Crocker.[13] He made an absolute distinction between pustular psoriasis and acrodermatitis perstans of Dore. There has been considerable recent literature on the subject, which need not be reviewed here.

The clinical picture of pustular psoriasis is usually consistent. There is a vesiculopustular squamous eruption, primarily affecting the thenar area of the palms and central inner portion of the soles and from these original sites spreading to adjacent areas. The pustules dry up; some form brownish translucent dots the size of a pinhead, and others form crusts or scabs and are desquamated, leaving a reddened, angry denuded epidermis. There are exacerbations and remissions. During an exacerbation there may be sensations of pruritus, heat and even dull "drawing" pain. Mycologic and bacteriologic examinations always give negative results. The condition may be accompanied by interdigital dermatophytosis which obscures the clinical picture.

In all but 3 of our cases there was concomitant psoriasis or a past history of psoriasis.

The histologic picture in these cases varies somewhat according to the condition of the horny layer and the age or stage of the condition. There was evidence of chronic eczema in 4 of the cases.

The vesiculopustules in the upper layer of the epiderm were filled with coagulated serum and some leukocytes. The rete pegs were irregularly acanthotic, and the acanthosis tended to include the suprapapillary plates. However, in all 9 cases there was an intense leukocytic infiltration of the upper portion of the cutis and also of the epiderm. This intense leukocytic infiltration appeared to be attracted to the surface of the epidermis, where small and large collections of leukocytes occurred, forming abscesses, which are best known as Monro-Sabouraud abscesses and may become large enough to be seen by the naked eye. These collections of leukocytes and degenerated epithelial cells occur,

10. Strandberg, J.: Acrodermatitis continua (Hallopeau), Acta dermat.-venereol. **6**:314 (Oct.) 1925.

11. Dore, S. E.: Notes on Cases of Chronic Mild Localized Type of Acrodermatitis Perstans, Brit. J. Dermat. **40**:12 (Jan.) 1928.

12. Hallopeau, H.: Sur la production, consécutivement à des plaques psoriasiques, d'achromies persistantes, Bull. Soc. franç. de dermat. et syph. **3**:11, 1892.

13. Crocker, H. R.: Diseases of the Skin, ed. 3, Philadelphia, P. Blakiston's Son & Company, 1903.

however, in other conditions than psoriasis and should not be taken as a pathognomonic criterion. They are frequently found in lesions of eczema, and recently Sulzberger [14] found that the application of extract of poison ivy to sensitized guinea-pigs will produce typical Monro-Sabouraud abscesses. This observation at least proves that this particular phase of the psoriatic picture can be of exogenous etiology. The explanation for this phenomenon was best described by Civatte.[8] A group of migratory cells emerge from a vessel at the summit of a papilla and open a passage through the rete mucosum which is disintegrated by their transit. At the point where this is about to occur, the malpighian cells become swollen and mass together. Their borders become less distinct, and there is considerable intercellular edema. It follows, then, that the dictum of Sabouraud—that the exocytosis of psoriasis is dry and without exoserosis—cannot be fully accepted. In this swollen and softened mass emigrated cells dig a sort of tunnel toward the surface, by which they ascend toward the upper layers of the rete. This tunneling is not the only way exocytosis takes place. Throughout the area polymorphonuclear leukocytes are seen between the swollen epithelial cells which form the walls of the tunnel, ascending the softened rete layer without tearing it. Having reached the upper malpighian layer the migratory cells encounter a barrier formed by the more or less keratinized layers, and the cells spread out like a column of smoke held down by an obstacle.

In our other 6 cases, constituting 66 per cent of the group, there were positive signs of psoriasis. Dr. David L. Satenstein, to whom we are indebted for help in the examination and interpretation of the histologic sections used in this work, holds that pustular psoriasis is a misnomer and that the picture is that of chronic eczema and not one of psoriasis. Many others also hold this view. Andrews and his associates [15] expressed the opinion that the histologic picture is not distinct enough for one to make a diagnosis without other signs of psoriasis being present. On the other hand, Dr. Alexander Fraser, who also gave us his interpretation of the histologic sections in this work, believes definitely that these cases of pustular psoriasis can be diagnosed histologically. It should be noted that he has been able to demonstrate this many times.

The high papillae and very thin suprapapillary plates coupled with the extreme dilatation of the vessels, the parakeratosis, which is patchy and intermittent, and, finally, the collections of pus lead us to believe that pustular psoriasis is a definite type and belongs with the syndrome

14. Sulzberger, M.: Personal communication to the authors.

15. Andrews, G. C.; Birkman, F. W., and Kelly, R. J.: Recalcitrant Pustular Eruptions of Palms and Soles, Arch. Dermat. & Syph. **29**:548 (April) 1934.

of psoriasis as one of its many manifestations. Its name is not material; any name linking it to psoriasis is sufficient.

5. *Lesions of Intertriginous Nature.*—Nine cases were studied. The lesions may be described for the most part as being erythematous, eczematoid, macerated and often fissured, occurring in the usual intertriginous areas, notably beneath the breasts, in the crural region and in the intergluteal fold. In our experience such intertriginous lesions occur much more frequently in cases of psoriasis than in cases of other cutaneous disorders.

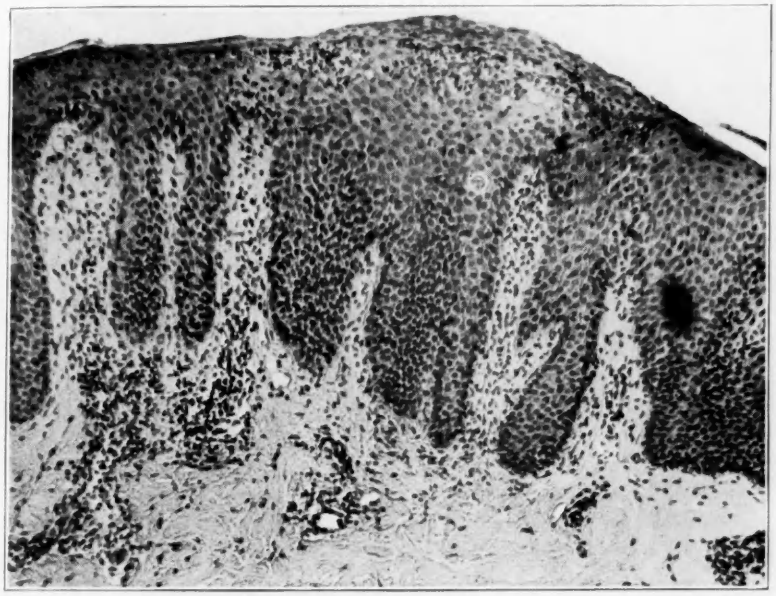

Fig. 5.—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type plus parakeratosis simulating chronic eczema.

The sections observed, although the condition in practically all the cases was diagnosed as chronic eczema, did have many features of psoriasis. However, the pathologic picture had been altered, so that in 30 per cent of the sections spongiosis and vesiculation were noted even though the granular layer was intact throughout other portions of the slide. Therefore, the condition in this group at least will have to be classed histologically with the eczemas primarily. It is interesting to note that in some of the cases, in which a typical psoriatic patch extended into the intergluteal fold, a section taken from the macerated area showed a histopathologic picture corresponding to the picture of eczema seen in other sections.

6. *Lesions of a Papulo-Erythematosquamous Nature.*—A study was made of 9 cases. The lesions included ill defined erythematous, dry, scaly lesions of polymorphic clinical character which loosely resembled those of parapsoriasis.

These lesions, although clinically resembling each other, had extremes in pathologic pictures, ranging from practically no histologic changes through eczema into the dry type of lesion found in neurodermatitis. Therefore, this group will be discussed more in detail with the summation of observations on the aberrant lesions.

7. *Lesions of Lichenoid Character.*—Eight cases were studied. This group included cases of lesions simulating lichen planus and the other

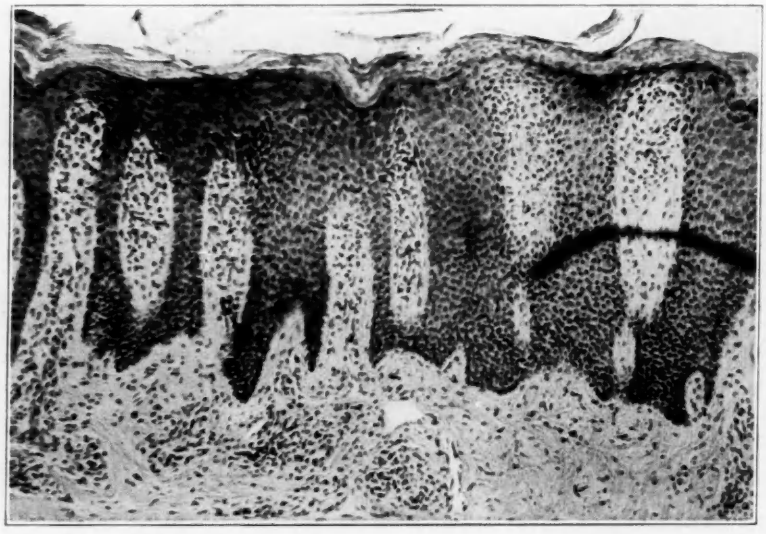

Fig. 6.—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type plus parakeratosis plus characteristic dilated vessels and papillary bodies simulating psoriasis.

lichens, including pityriasis rubra pilaris. There were 3 cases of concomitant lichen planus with long-standing psoriasis. In 1 case there was a history of lichen planus-like papules occurring each spring over a period of several years; many cases of this type have been reported. The pathologic picture of the lesions of lichen planus was that of typical lichen planus. However, the sections of lesions on the elbow in 2 cases showed the histologic architecture of chronic eczema, although the clinical picture was that of typical psoriasis. In the third case the specimen studied showed the structure of lichen planus. This phenomenon will be discussed later, under altered cutaneous resistance.

Pityriasis rubra pilaris has many features in common with psoriasis, with which it coexists or alternates often at its inception. We found coexisting pityriasis rubra pilaris in 1 case, with typical psoriasis elsewhere. Other cases have been reported by Wigley, Little,[16] Davis, Drosty and Prieto.[17]

The lesions in this group presented a variety of histologic pictures; however, they were all dry, a well developed granular layer predominated and in some sections parakeratosis was present but sparse. The papillary and subpapillary zones showed moderate lymphocytic infiltra-

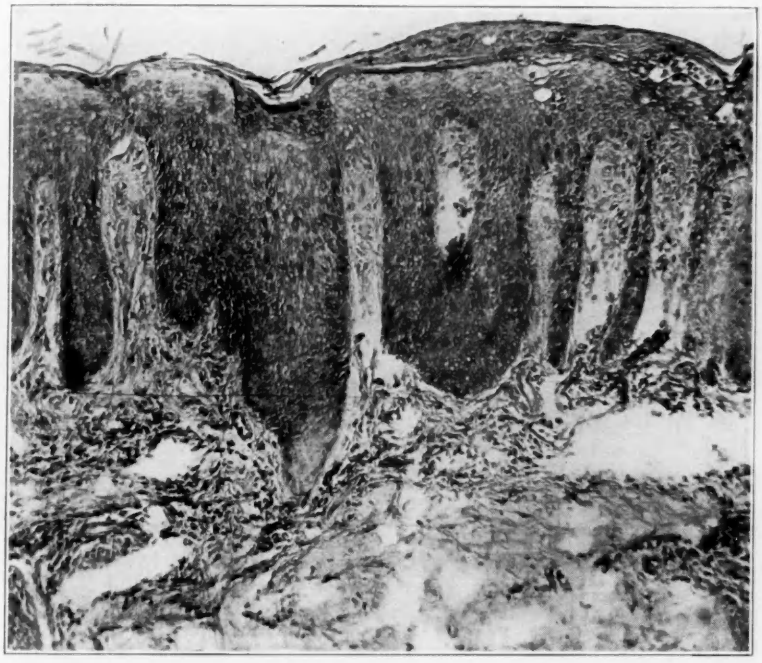

Fig. 7.—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type plus parakeratosis plus characteristic dilated vessels and papillary bodies plus exfoliation of the epidermis (exfoliative dermatitis).

tion except in the 3 cases of typical lichen planus, which were excluded from this summation. The cause for the variation in histologic structure in similar clinical lesions will be discussed later.

16. Little, G.: Psoriasis Simulating Lupus Erythematosus, Tr. M. Soc. London **30**:384, 1906-1907.

17. Prieto, J. G.: Relation of Psoriasis to Pityriasis Rubra Pilaris: Case, Actas dermo-sif. **26**:345 (Feb.) 1934.

8. *Lesions of a Nodular Character.*—The nodular lesions were studied in 5 cases which comprise the group in which the lesions were distinctly infiltrated, nodular and even fungoid. One of these cases was that of a private patient of Dr. Frank Fraser and Dr. Alexander Fraser, who was presented before the New York Dermatological Society and who had typical mycosis fungoides on what appeared to be psoriasis of many years' duration. (This case will be reported in detail by them later.) However, we can say that several specimens had been taken from this patient in the past, and all had shown only psoriasis, with no evidence of mycosis fungoides. Nodular lesions have a predilection

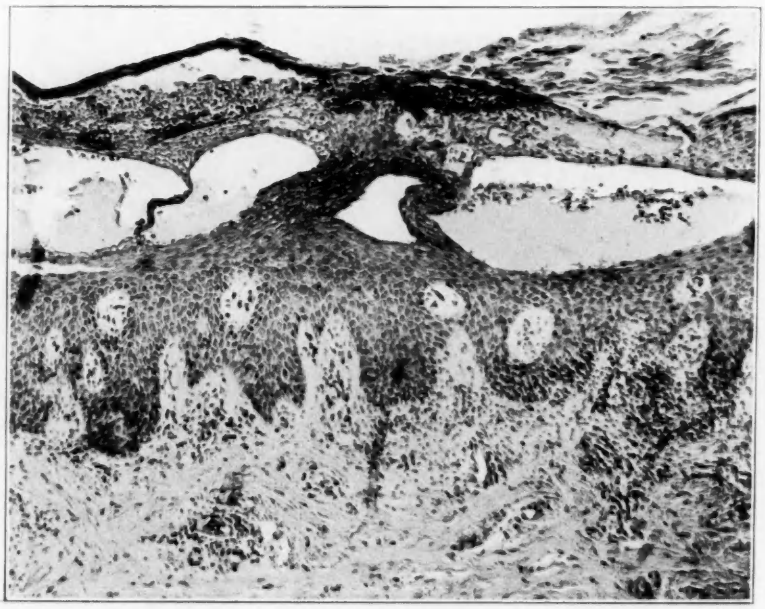

Fig. 8.—Photomicrograph of pustular psoriasis of the palms associated with typical psoriasis elsewhere.

for the extremities, although occasionally one may be found on the trunk. The histopathologic change is not sufficiently distinctive to place the cases in a separate group entity. The lesions in our cases had features of eczema, 50 per cent showing spongiosis and formation of vesicles. A characteristic feature of psoriasis is severe edema of the papillary bodies and upper and middle portions of the cutis, with a tendency to regular acanthosis of the rete pegs. Therefore, again we had a group of cases in which the condition did not resemble psoriasis completely yet retained some of its main features.

9. *Lesions of Palms and Soles Suggesting Keratoderma.*—In 4 cases of 100 there was a characteristic thickened, rough, somewhat verrucous appearance of the palms and soles. Clinically the condition resembled true keratoderma palmare et plantare. There was typical psoriasis elsewhere in all cases.

The characteristic feature of the sections was a greatly thickened hyperkeratotic layer with a well developed granular layer. In 1 section small vesicles without spongiosis were noted at the summit of the rete peg. The rete pegs were regularly acanthotic in 75 per cent of the sections, with the papillary bodies remaining comparatively normal, giving the appearance of elongated papillae. There were features of psoriasis and also features which suggested keratoderma palmare et plantare. In 1 case vesicles were present without spongiosis.

10. *Lesions Resembling Lupus Erythematosus.*—Two cases were studied histologically. The lesions simulated the clinical characteristics of lupus erythematosus. They were sharply defined, oval or circinate, erythematous, slightly scaly patches of various sizes. Frequently, owing to an element of seborrhea, the clinical diagnosis became difficult. In 1 case the section showed typical lupus erythematosus, with thinned epithelium, basophilic degeneration, loss of elastic tissue and edema of the cutis. In the other the lesions were those of the dry type of chronic eczema.

11. *Exfoliative Dermatitis Following Psoriasis.*—Two cases were studied. There was marked resemblance to the picture of psoriasis with an increase in mitotic figures in the epidermis and an increased infiltration of lymphocytic cells and connective tissue cells in the papillary and subpapillary zone. The picture was not distinctive and could not be differentiated from that of exfoliative dermatitis resulting from eczema, pityriasis rubra pilaris or any of the other conditions eventuating in exfoliation.

## COMMENT

Over 600 patients were thoroughly examined for aberrant lesions, and among this number 100 were found with lesions abnormal enough to be placed in one of the groups described. Therefore, we found on the average 1 patient of 6 presenting aberrant lesions of psoriasis with typical lesions elsewhere.

To summarize briefly the total observations on the aberrant lesions, we found that there were several clinical groups in which a somewhat uniform histologic picture was present, subject to slight variations. The group with eczematous characteristics presented superficial dermatitis with eczematoid changes. The lesions presented by the group with seborrhea were drier than those of the group with eczema but still showed signs of eczema. In 24 per cent of the cases vesiculation was

present and in 15 per cent, spongiosis. The granular layer was prominent in most sections. The lesions of the group with circumscribed neurodermatitis were uniform, with an increased granular layer, but the histologic picture of the papillary bodies and subpapillary layer varied greatly, ranging from no change to greatly dilated vessels and interstitial edema. In 4 of the cases of pustular psoriasis there was a picture of acute eczema with intense exudation, and in the remaining 5, an almost classic picture of psoriasis. The lichenoid, papulo-erythematosquamous, keratoderma, lupus erythematosus, nodular and exfoliative types were greatly in the minority in frequency of occurrence, and the histologic pictures were polymorphic.

In 1 case the nodular lesions deserve special mention. The patient for many years had had what had been diagnosed by many competent dermatologists as psoriasis. The lesions were not pruritic but became so following roentgen therapy. A specimen was taken for section in February 1935, and the slide showed psoriasis. Two weeks later, fungoid lesions appeared in several areas, and sections from these areas gave a picture of mycosis fungoides characterized by mitotic figures and irregularity of size, shape and staining qualities of the nuclei and protoplasm of the newly formed reticular cells. There was a definite reticulum about each of the cells. We call attention to this phenomenon of mycosis fungoides occurring in patients with clinical psoriasis because since the study was begun, many dermatologists have commented on this singular occurrence in their own experience. A considerable number of cases of this type have been reported. Therefore, it must occur more frequently than is generally supposed.

Keeping in mind local and external modifying influences on the disease in the same patient, it seems impossible that most of the atypical lesions were not related in some way to the typical psoriasis which each patient had. Therefore, it would seem logical that the aberrant lesions offer a connecting link between psoriasis and the other superficial inflammatory dermatoses. Surely the soil and etiology in many instances were the same for the aberrant as for the typical lesions. Many of the aberrant lesions had the typical distribution of psoriasis, and their evolution presented the same physiologic problems.

We are forced to assume that the difference in the clinical and in the histopathologic picture lies in one or more of the following causes:

1. The pressure resistance of the various anatomic segments of the skin had become altered, changing the clinical and the histologic picture.

2. We were dealing with a transient stage of psoriasis.

3. There was an unusual or altered concentration and distribution of the toxic principle.

4. There were variations in local resistance, due to the site of the lesions or to exogenous causes, such as friction, moisture, heat and treatment.

If it is possible to have one or more aberrant lesions caused by any one of the aforementioned causes, is it not possible to have the same factor act generally and change the entire clinical picture but still have the same fundamental etiologic factor?

Heimann [18] stated that eczema does not differ from the other fibrinous lymphocytic inflammations except in the histologic peculiarities occasioned by its site.

Psoriasis, by reason of its fixed clinical and histopathologic picture, is the normal reaction to an abnormal stimulus, and by the same reasoning we can say that eczema, because of its polymorphic character, is a variation from the normal reaction. Therefore, psoriasis is not a disease but a cutaneous reaction governed by the factors previously mentioned. This applies equally to the other superficial dermatoses. Psoriasis, although not a disease, is an entity because of its fixed type of cutaneous reaction, giving in the majority of cases a typical clinical and histologic picture.

A classification according to the following outline is consistent with the actual histopathologic findings of the aberrant lesions:

1. Superficial dermatitis with no epidermal changes (simple dermatitis).

2. Superficial dermatitis plus eczema.

3. Superficial dermatitis plus epidermal changes of the dry type simulating neurodermatitis.

4. Superficial dermatitis plus epidermal changes of the dry type plus an occasional vesicle (seborrheic dermatitis).

5. Superficial dermatitis plus epidermal changes of the dry type plus parakeratosis (chronic eczema).

6. Superficial dermatitis plus epidermic changes of the dry type plus parakeratosis plus characteristic dilated vessels and papillary bodies (psoriasis).

7. Superficial dermatitis plus epidermal changes of the dry type plus parakeratosis plus characteristic dilated vessels and papillary bodies plus exfoliation of the epidermis (exfoliative dermatitis).

All the aforementioned histopathologic features are seen in cases of psoriasis and its atypical manifestations in which the history and clinical

18. Heimann, W. J.: Histopathology, J. Cutan. Dis. **34**:203 (March) 1916; Histopathology of Lichens: Lichenifications and Neurodermatitis, ibid. **35**:28 (Jan.) 1917.

findings are beyond question diagnostically. The histopathologic changes vary with the type of lesion. The lesions vary according to the alteration in the balance of the various factors of resistance of the skin.

Weeping without vesiculation takes place by the exudation of serum from the dilated intercellular spaces, the flow of which meets no resistance by the parakeratotic scale. Therefore, when this flow is retarded by the increased resistance of the upper layer of the epiderm vesicles are formed in the area of least resistance.

The genesis of the vesicle depends on edema. The actual cause of edema is not known, but it seems to be due to a serotaxis in response to an irritant. There appears to be a difference of opinion among authorities as to whether edema is primarily intercellular or intracellular. Unna stated that it is intercellular, whereas Leloir expressed the opinion that it is intracellular, and Darier stated that both conditions occur together. Purely from a physical basis, the latter opinion would appear the most logical.

In eczema there is a more active exciting cause or an abnormal reaction producing spongiosis and vesiculation, whereas in psoriasis the exciting cause is less potent, and a slower, more stable, tissue reaction usually takes place, causing the same picture but ordinarily without spongiosis and vesiculation.

It appears that in all cases the area adjacent to the lesion is somewhat affected by the process. It is possible that when a heavy granular layer is present the eruption is limited to smaller areas because of an increased suprapapillary resistance, and an entirely different picture is produced.

There is no one feature of psoriasis that cannot be found in the other superficial inflammatory dermatoses. There is no absolute pathognomonic histopathologic criterion in psoriasis. However, when both the histologic and the clinical findings agree in the majority of details the condition should be classed with the superficial inflammatory dermatoses under the descriptive title psoriasis.

SUMMARY

A basic histopathologic formula is developed from a study of biopsy specimens taken from clinically typical psoriatic lesions of 50 patients.

The aberrant lesions are placed in convenient clinical groups, and a brief description of the histologic abnormalities is given.

The incidence of aberrant lesions in psoriatic patients is approximately 1 in 6.

A simple histologic classification of the aberrant lesions is given.

## CONCLUSIONS

There were certain features of the study which were impressive enough to be recorded.

1. Psoriasis cannot be unequivocally diagnosed from observations of a histologic section without considering the clinical findings.

2. The aberrant lesions link psoriasis definitely as a fixed phase of a superficial dermatitis which may have the same etiologic factor as exfoliative dermatitis on the one hand or seborrheic dermatitis, eczema, neurodermatitis, etc., on the other.

3. The histopathologic architecture tends to change in conformity with the evolution of the clinical lesion.

Drs. David L. Satenstein, Alexander Fraser and Frank Fraser assisted in the examination and interpretation of the histologic material.

We present this report without offering a final conclusion. The subject is open for, and requires, further study. We hope that others may be encouraged toward a similar line of investigation. Eventually it may help to evolve a new and better concept of the pathogenesis of many cutaneous disorders.

## ABSTRACT OF DISCUSSION

DR. CLARK W. FINNERUD, Chicago: I believe that this study deals largely with the histopathologic and clinical variants of psoriasis, rather than with histogenesis. With regard to the histogenesis of the disease, the observations carried out by Dr. Ebert in our laboratory tend to support the theory stressed by Kyrle that psoriasis is primarily an epitheliosis and that it may be produced by a virus of some kind acting on favorable soil. In a case of acute psoriasis, histologically and clinically characteristic, a scratch mark was made, and forty-eight hours later a part of this was excised. Kyrle's acidophilic cytoplasmic inclusion bodies, similar to the Guarnieri bodies of variola, were readily demonstrated. These were extruded from the nucleus and nucleolus into the cytoplasm. The initial and sole change at this time appeared to be in the epidermis. Control Köbner scratch marks gave negative results. The presence of psoriasis does not preclude the occurrence of other cutaneous diseases. Every one has seen other cutaneous involvements occurring in association with psoriatic disorders, some of which may somewhat resemble psoriasis. On the other hand, psoriasis may cause lesions of varying clinical and histologic character, resulting, among other factors, from the varying architecture of the skin in different parts of the body. It has been my experience that a disease which simulates another clinically also commonly tends to simulate it microscopically. For instance, one sometimes sees a patient with a clinical picture suggesting a questionable diagnosis of lupus erythematosus or lichen planus, and one finds that the lesions even simulate each other histologically, whereas ordinarily they do not. As stated by Dr. Foster, there are no pathognomonic histologic observations in psoriasis, although some occur more consistently than others. No one process exists in the lesions that does not occur at times in the lesions of certain other dermatoses. From the evidence presented, I cannot consider psoriasis as anything but a clinical entity. This disease, like syphilis, erythema multiforme, dermatitis venenata and various other diseases, is capable of producing various clinical and histologic pictures.

DR. FRED WISE, New York: There is a group of dermatologists, especially British, who regard psoriasis and seborrheic eczema as different manifestations of the same disease, which opinion has considerable bearing on this subject. If one regards psoriasis as a tissue reaction of the skin resulting from an insult or a combination of various provocative factors instead of from only one factor attacking the predisposed skin as a whole, one can conceive of at least a partial explanation for the occurrence of atypical and aberrant lesions in psoriasis. Every dermatologist frequently encounters patients with eruptions about the genitals and intergluteal regions which on cursory examination are diagnosed as seborrheic eczema, ringworm or ordinary intertrigo, only to have the eruption prove to be psoriasis after longer observation or careful examination. It is probable that several diversified factors play a rôle in the formation of atypical lesions. Among these may be diet, sweat, friction, the use and misuse of water and of topical remedies and variations in temperature and climate. I think that even deterioration of the patient's general health and his physical and emotional upsets might act as possible causes for the production of atypical lesions. These unorthodox lesions have been studied by Jadassohn, who gave them the name "psoriasoid." In a recent article Robert Bernhardt (*Arch. f. Dermat. u. Syph.* **171**:322 [March 16] 1935) pointed out some of the differences between the lesions of Jadassohn's psoriasoid and those of typical psoriasis. In psoriasoid (1) chalky white scales do not appear on scratching; (2) on removal of the scale there is an absence of an epithelial membrane, the surface being smooth, glistening red and almost moist; (3) instead of punctate hemorrhage, punctate purpura appears, and (4) there is a punctate serous exudation in some of the aberrant lesions which does not occur in the scratched lesions of true psoriasis. This corresponds closely to the histologic appearances described by Dr. MacKee and Dr. Foster. Atypical clinical and histologic changes are encountered in many cutaneous diseases, among them syphilids, tuberculids, lichen planus, mycosis fungoides, various forms of lymphoblastoma, parapsoriasis, granuloma annulare and many other dermatoses.

DR. HERMANN FEIT, New York: I have recently been especially interested in the many so-called aberrant types of psoriasis, and I have seen cases in which the lesions resembled syphilis, dermatitis herpetiformis and the like. On examination I found that some of the lesions, especially those in single patches, represented epithelioma and lymphoblastoma. Dr. Foster said that one cannot make a definite histologic diagnosis of psoriasis. But one should make use of the method of Brocq, curettage of the scales layer by layer for about fourteen or fifteen layers, and then one would come to the famous pellicle of Buckley, who never found the condition in any other disease but psoriasis. I think that this method is too little used in making a definite diagnosis of psoriasis. Psoriasis is a cutaneous reaction, because there is nothing that cannot elicit an outbreak of psoriasis: Any mental or physical distress or any metabolic disturbance in a patient who has this peculiar type of condition will cause some psoriatic reaction. It would be better, perhaps, to call this atypical form of psoriasis psoriasiform dyskeratosis.

DR. GEORGE C. ANDREWS, New York: This paper clearly shows that one has not the right to call clinically atypical lesions psoriasis unless the histology is definite. This does not mean that I take the view that there is no such thing as pustular psoriasis of the palms and soles. However, I object to including cases of pustular eruptions on the palms and soles in which there are clinical lesions of psoriasis and the histologic changes typical of psoriasis are not present and in which there is no suspicion of psoriasis in the personal or the family history.

Whether the aberrant lesions described in this paper should be classified as psoriasis is not of as much importance as the effort to determine the etiology of psoriasis. Dr. Stokes recently spoke of an underlying cause and a precipitating cause in reference to rosacea. A similar conception applies to psoriasis and the aberrant lesions mentioned by Dr. Foster and Dr. MacKee. The predisposing condition in these cases is an underlying tendency to parakeratosis in some persons. This accounts not alone for the clinical features but also for similarities in the histologic observations in many of the sections studied by the authors.

Dr. David Bloom, New York: In 7 of 8 cases of pustular psoriasis the lesions presented the typical clinical features described in the literature by Barber and others. Specimens from 5 patients were examined microscopically: In 2 the typical histologic picture of psoriasis was present, and the pustules manifested themselves as a conglomeration of Monro abscesses situated between the corneous layer and the epithelial layer; in 1 case the histologic picture of psoriasis was present, with a large intradermal pustule, and in another case simple inflammation was seen. In the fifth case, in which the condition was diagnosed clinically as keratosis with the formation of pus, microscopic examination revealed typical psoriasis with the same intradermal pustule as was seen in 1 of the other cases. The clinical picture, the course, the extreme resistance to any treatment and the sterility on mycologic and bacteriologic examination make pustular psoriasis a disease entity. Its frequent association with typical psoriasis elsewhere on the body and the previously described histologic observations justify the name pustular psoriasis. The study of atypical lesions may give a clue to the etiology of this mysterious disease.

Dr. Adolph B. Loveman, Louisville, Ky.: Within the past year I carried out autogenous skin transplants in a case of psoriasis. These were grafts of full thickness, carried out with the patient under general anesthesia. I hope to repeat this experiment at the first opportunity. The results appear to coincide with those reported by Sulzberger and Wise in cases of eruptions caused by phenolphthalein. The psoriatic lesion transplanted to normal skin did not cause psoriasis; but I believe that the normal skin transplanted to the psoriatic patch did become psoriatic. By observing these grafts frequently I had an opportunity to study some of the other lesions and in doing so observed another similarity to certain types of drug exanthems, namely, that psoriasis apparently is a fixed eruption. The lesions seem to return in the identical location in which they previously existed. If this is true and if the experiment with autogenous skin transplants can be repeated and verified, I believe that I have evidence that psoriasis is a systemic disease manifesting itself on the skin as a result of a hematogenous spread.

Dr. Marion Sulzberger, New York: This is probably the largest consecutive series of cases of typical and atypical psoriasis ever carefully investigated histologically. I have always been of the opinion that psoriasis is a more or less polymorphic disease, presenting many atypical lesions and in some instances an entire picture which is atypical. How many times does one find in a normal person in a nondermatologic group an eczematous patch, a patch of neurodermatitis or some other chance dermatologic finding? Does one find such an associated, but not necessarily connected, dermatosis in 1 of every 6 patients who present themselves to a gynecologist or to an ophthalmologist, or even in 1 of 6 patients with acne? If one includes such almost universal diseases as intertriginous ringworm, mild acne and pityriasis of the scalp, one will find such diseases in 1 of 6 normal controls. However, these are not exclusively the conditions to which the authors have alluded, and one must come to the conclusion that there is some obligatory connection between the presence of at least some of the atypical lesions

and the psoriasis. What is the connection? One hypothesis is that these are psoriatic lesions altered for some unknown reason by the soil or by individual predisposition. That, I think, is manifestly true of a certain percentage of the lesions described. It is logical to assume that seborrheic dermatitis-like and intertriginous lesions are altered psoriatic lesions, although the histologic observations are atypical. There is another type of lesion described by the authors which is probably not an altered lesion of psoriasis, but which occurs in increased incidence in psoriatic patients. To explain this one must hypothesize that the patient with a tendency to psoriasis has a weakened integument, which has in some way increased his susceptibility to the other dermatosis. It would be easy to suppose that the psoriatic scale may be more permeable than the normal horny layer and may therefore allow the penetration of sensitizing substances. The scale may also form a culture medium for pathogenic or saprophytic organisms which multiply and thereby produce hypersensitivity to fungi and bacteria. I am inclined to believe that these two explanations are correct, that some of the concomitant lesions described by Dr. Foster and Dr. MacKee are altered psoriatic lesions and that some of them are supervening lesions of other dermatoses to which the psoriasis has in some way predisposed the patient. One must also consider the possibility of psoriasis supervening on the actual areas irritated by another dermatosis, or, vice versa, another dermatosis appears at the actual site of a psoriatic irritation, as in the isomorphic irritant phenomenon of Köbner.

Dr. Paul D. Foster, Los Angeles: That there are concomitant cutaneous conditions in psoriasis is true, but I believe that the high percentage of aberrant lesions found in patients with typical psoriasis, as shown by those with the five main types, that is, eczema, seborrheic dermatitis, neurodermatitis or chronic lichenified eczema, pustular psoriasis and erythematosquamous dermatitis, occur more frequently in patients with psoriasis than in the usual group of patients with cutaneous diseases or in any other given group of patients. Jadassohn did some excellent work on the psoriasoids, but I do not find a connection between his work and ours. It seems to me that the patients he studied had more atypical psoriasis; he studied the problem in patients with borderline differentiation, while we studied atypical lesions of patients with typical psoriasis. Dr. Andrews said that one has no right to make a diagnosis of pustular psoriasis without lesions of psoriasis elsewhere. Dr. MacKee and I are unable to support this contention. In 6 of the cases that we studied psoriasis was present on other parts of the body and in 3 it was not. In the 3 cases in which psoriasis was present the condition was classified as pustular psoriasis because of the typical picture presented in the histopathologic section plus the clinical details that have been emphasized by Barber, MacKee, Bloom and others. We believe that it is possible to diagnose the condition clinically in most cases of localized psoriasis on any part of the body, even on the nails alone. Typical pustular psoriasis of the palms and soles can be diagnosed clinically as such in the majority of cases by those who have had experience, regardless of the lesions on the rest of the body. In pustular psoriasis the formation of the pustules is a simple matter. Dermatologists are familiar with the formation of the Monro-Sabouraud abscesses, the tunneling, the insinuation of the leukocytic cells into the epiderm and the exocytosis and exoserosis into and through the epithelium beneath the corneous layer; and in most cases of psoriasis, that is, in the typical lesions, the parakeratotic layer and the corneous layer are loose enough to allow these cells to be desquamated with the scale. On the palms and soles is a thick hyperkeratotic layer, a barrier holding down the excretion of these substances so that beneath the hyperkeratotic layer is a collection of the leukocytes and the degenerated epithelial cells to form the lakes of pus, giving a different clinical picture. Dr. Loveman's observation opens new channels for investigation.

# ANTISYPHILITIC TREATMENT

## EFFECT OF REST ON THE RESULTS OF TREATMENT AND THE GENERAL BENEFIT DERIVED FROM THERAPY

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The problem expressed in the title of this paper has been given little consideration in modern syphilologic literature. Among the modern textbooks only that by Stokes [1] gives adequate consideration to a discussion of the paramount necessity of rest as an adjunct to specific treatment, while others have little or nothing to say. Even less can be found about the general effect of specific treatment on the patient. Yet the distinct influence which antisyphilitic treatment has on the patient's general well-being must be apparent to every experienced syphilologist. To a certain extent this influence can be objectively evaluated, for example, by the increase in the patient's weight. There is, however, a less tangible, but none-the-less important, change which can be observed in the majority of the patients, namely, a distinct improvement in the subjective feeling of well-being. In cases of latent syphilis the difference between the way the patient feels before treatment has been given and his condition after it has been administered for some time has been so especially striking that we thought it advisable to give this problem further consideration. The object of our endeavor was to evaluate the various factors which might be responsible for both subjective and objective improvement in the majority of our patients and for lack of improvement in the minority.

The general beneficial effect of antisyphilitic treatment is caused by the following factors:

1. *The specific effect of antisyphilitic drugs.* This needs no explanation. It is readily understood that elimination (in toto or in part) of a chronic infectious process will result in an improvement of the general well-being of the patient.

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From the Section of Dermatology of the Department of Medicine, University of Chicago. Read at the Scientific Session of the Section of Dermatology, June 7, 1935.

1. Stokes, John H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

2. *The nonspecific effect of antisyphilitic drugs.* This seems to play a negligible rôle as far as compounds of mercury and bismuth are concerned but is a definite factor in the case of the arsenical compounds. The arsphenamines are of distinct value against a number of non-spirochetal conditions, e. g., tuberculosis of the skin, blastomycosis and multiple sclerosis. Their tonic action—undoubtedly due to their arsenic content—form a welcome addition to the effect of treatment. This tonic action is most pronounced in patients treated with tryparsamide, in whom considerable gain in weight is to be expected. In addition, tryparsamide is a mild aphrodisiac, most welcome in raising the spirit of the discouraged and depressed tabetic patient.

3. *The effect of nonspecific treatment.* It has been realized for a long time that it is a serious mistake to treat syphilis merely chemically. Syphilis shows many parallels with tuberculosis, so close that even microscopic examination sometimes cannot differentiate the clinical manifestations of the two diseases; the continuous fight between the defense mechanism of the host and the virulence of the etiologic agent is common to both. It is now definitely recognized that resistance-building measures, especially rest, are necessary in the treatment of tuberculosis. This is just as important in the treatment of syphilis, in which the results of poor therapy are more remote and not as dramatic as in tuberculosis. During the prearsphenamine era this was well understood by the syphilologists; vacations at spas, hot water, steam and sulfur baths and stimulation via the gastro-intestinal tract (with a compound decoction of sarsaparilla) were in general use. Primitive people (African Negroes in Assuan) have been treating syphilis with symptomatic success by burying the patient for several days in hot desert sand and administering decoctions.

With the advent of the arsphenamine era all the empirical achievements of additional nonspecific treatment of syphilis were momentarily forgotten. The overwhelming "chemical success" ruled the development of methods of treatment. Yet, as has occurred in the practice of medicine throughout the ages, the pendulum was bound to swing back. During the past decade extensive research, both on human beings and on animals, has put the empirical knowledge of nonspecific treatment on a more scientific basis. The tissues react against the invasion by Spirochaeta pallida by a process termed *Umstimmung* (Pirquet). This resistance phenomenon represents, teleologically speaking, the curative endeavor of the organism (Bloch). We are able to bring about an important increase in this mechanism of defense by nonspecific

physical or chemical therapy. The work of Rajka and Radnai [2] and of Gottron [3] shows that systemic ultraviolet irradiation has a distinct influence on the involution of syphilitic lesions. In combination with autohemic injections, resistant syphilis, including the so-called serologically fast syphilis, has been successfully treated. The course of experimental syphilis in rabbits has been materially influenced by sunlight (Brown and Pierce).[4] Stimulation of the esophylactic properties of the skin was successfully tried in the form of experimental inunctions with ointments not containing mercury by Jarisch,[5] Salomon and Hübner, and Hoffmann.[6] The results did not differ materially from those following ordinary mercurial inunctions. The beneficial effect of the treatment of syphilitic patients in spas has been found to be due to a combination of several factors: In some of the spas the direct action of heat (hot springs) and perspiration must be considered. This is in accord with the results of experiments with rabbits by Weichbrodt and Jahnel,[7] Schamberg and Rule [8] and Frazier,[9] who observed the more rapid disappearance of syphilitic lesions of all stages after treatment with hyperpyrexia than after the use of mercury. Other factors are rest, change of climate, stimulation of metabolism and stimulation of the skin as an organ, presumably causing a beneficial reaction on the sympathetic nervous system. Here we may also mention that gymnastics, massage and outdoor exercise are of recognized value in the treatment of tabes. It is not within the scope of our study to go into the wide and successful aspects of the various methods of therapy with non-

2. Rajka, E., and Radnai, E.: Ueber die günstige Beeinflussung der Wa. R. und Neurosyphilis mit Licht-, beziehungsweise mit kombinierter Licht- und Eigenblutbehandlung, Compt. rend. Cong. internat. de dermat. et syph., 1931, p. 995.

3. Gottron, H., in discussion on Rajka and Radnai.[2]

4. Brown, Wade H., and Pierce, Louise: The Influence of Light on the Reaction to Infection in Experimental Syphilis, J. Exper. Med. **45**:497 (March) 1927.

5. Jarisch: Therapeutische Versuche bei Syphilis, Wien. med. Wchnschr. **45**: 721, 1895.

6. Quoted by Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 18.

7. Weichbrodt and Jahnel: Einfluss hoher Temperaturen auf Spirochaeten und Erscheinungen der Lues im Tierexperiment, Deutsche med. Wchnschr. **45**: 483, 1919.

8. Schamberg, Jay Frank, and Rule, Anna M.: Therapeutic Effect of Hot Baths in Experimental Primary Syphilis in Rabbits, J. A. M. A. **88**:1217 (April 16) 1927.

9. Frazier, Chester N.: Effect of Elevation of Body Temperature on the Course of Experimental Syphilis in the Rabbit, Arch. Dermat. & Syph. **16**:445 (Oct.) 1927.

specific protein and with fever. We wish to mention, however, that we have also found the combination of generalized ultraviolet irradiation and injections of autogenous blood a valuable aid in converting persons with a tendency to relapse into normally reacting patients.

4. *The patient's habits and ways of living.*—Any one afflicted with a constitutional chronic infectious disease should live according to a certain regimen if he expects the full benefit of medical treatment. Patients with syphilis are no exception to this. Stokes [1] said: "Rest is one of the potent, and often life-saving factors in the general management of the syphilitic patient. More and more frequently in the recent literature one encounters the theory that loss of resistance to the disease and failure to make therapeutic headway against it are functions of the exhaustion of the defence mechanism, including presumably the reticulo-endothelial system and the antibody-forming agencies, a loss of function which may be recovered after rest." Normal sleeping hours, a nap after luncheon, reduction of mental and emotional strain and regular vacations, spent preferably in the country, are essential additions to the specific treatment. The diet presents another point of attention. Since constitutional syphilis is associated with marked consumption of proteins, the diet of the patient should be rich in calories and especially in proteins.

Thus far we have been better aware of the deleterious consequences which follow the breaking of the outlined rules than of the beneficial effects if they are conscientiously obeyed. For instance, it is known that the victims of dementia paralytica are frequently high-strung business men of the "neurocirculatory instability" type described by Becker.[10] The onset of tabes often follows periods of stress. The peripatetic patient (Moore [11]) of the traveling salesman type has a poor prognosis because of the absence of a regulated life. Heavy physical exertion predisposes to aneurysm. The indiscriminate use of alcohol has long been known to delay progress and to produce relapse. Excessive use of tobacco predisposes to leukoplakia. All in all, the bad effect of wear and tear is too definite to be doubted.

It should not pass unmentioned, however, that the striking improvement in the feeling of general well-being, as brought on by the various

10. Becker, S. W.: Dermatoses Associated with Neuro-Circulatory Instability: Generalized and Localized Pruritus, Neurodermatitis, Dyshidrosis, Urticaria and Angioneurotic Edema, Lichen Planus, Neurotic Excoriations, Alopecia Areata, Dermatitis Herpetiformis and Scleroderma, Arch. Dermat. & Syph. **25**:655 (April) 1932.

11. Moore, Joseph Earle: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas. Publisher, 1933.

factors which we have discussed, may sometimes be a drawback. In fact, the patient who experiences the general benefit of the treatment is frequently only too likely to minimize the danger of the disease and to consider himself cured at a time when he is going through the most critical period of his infection.

## INVESTIGATIONS

Our study was carried out by supplying each patient with the questionnaire shown in table 1. The lower portion was filled out by the patient, and data for the upper portion were obtained from the patient's record.

TABLE 1.—*Questionnaire*

Name..... Date.....
Sex.....Age..... Unit No.....
Weight before treatment.....
Weight at present time or one year after beginning of treatment.....
Diagnosis .....
Serologic peculiarities.....
(e. g. Wassermann-fast, persistently + spinal fluid, serologic relapses)
Clinical symptoms due to syphilis.....
(e. g. gastric crises, impairment of vision)

We would appreciate it if you would answer the following questions:

What kind of work do you do?.....
How many hours daily?..... How many days weekly?.....
Do you take a vacation every year?..... How many weeks?.....
How do you spend your vacation?.....
.....
How do you spend your week-ends?.....
Do you take any form of exercise?.....
Do you keep regular sleeping hours?..... How many hours?.....
Do you take a nap after luncheon?.....

How did you feel before treatment was started?.....
.....
Do you feel differently now?.....
How long did you take treatment before you noticed this change?.....
How do you feel now?.....

Questionnaires were sent to 500 patients chosen at random, who were of all ages and in all stages of syphilis and who had been treated for at least one year. Answers were received from about one half of this number. Several questionnaires had been filled in in such a way as to make correct evaluation impossible. After these were discarded, 236 answers remained, on which this study is based. Since our institution is a pay clinic, the patients were in general of a higher type than can be found at the free dispensaries. The social stratum may be said to correspond with that of the patients of the city practitioner.

The questionnaires were separated into three groups according to the statements made by the patients.

| | | | |
|---|---|---|---|
| Feeling of general well-being improved..... | 171 | 72 per cent | Group I |
| Feeling of general well-being not improved..... | 53 | 22 per cent | Group II |
| Feeling of general well-being impaired..... | 12 | 5 per cent | Group III |

In order to study the influence of the patients' habits and ways of living, the patients of each group were classified into one of three classes:

1. Regular and relaxed. Only such patients were included as stated that their working hours were not longer than nine hours per day, that their sleeping hours were regular and not less than eight hours and that they took a vacation every year.

2. Moderately resting. Patients in this class had stated that their working hours were not longer than nine hours per day, that their sleeping hours were regular and not less than eight hours but that they took no vacation or that they had less than eight but not less than seven hours of sleep and took a yearly vacation.

3. Nonresting. Patients in this class stated that they either had abnormally long working hours, kept irregular sleeping hours or had six hours or less of regular sleep and, for the most part, took no vacation.

For simplification we shall refer to these classes as rest plus, rest normal and rest minus. Our three groups of patients were thus analyzed as table 2 shows.

The information given in table 2 is obvious. The patient who has had a better regulated life has obtained the best symptomatic improvement. This effect becomes even more apparent if the results are analyzed according to the clinical form of syphilis treated. Thus it was found that of the rest plus patients of group III, one had dementia paralytica, one suffered from late vascular syphilis and chronic degenerative arthritis and one was Wassermann-fast, with involvement of the central nervous system. This explains the lack of improvement in the rest plus patients in group III.

TABLE 2.—*Number and Percentage of Patients from Each Group*

| | Rest + | | Rest N | | Rest − | |
|---|---|---|---|---|---|---|
| Group | No. | Percentage | No. | Percentage | No. | Percentage |
| I | 42 | 25 | 79 | 46 | 50 | 29 |
| II | 11 | 20 | 11 | 20 | 31 | 60 |
| III | 3 | 25 | .. | .. | 9 | 75 |

These experiences are in line with the observations of one of us (S. W. B.) that the results of treatment at the Mayo Clinic, where the patients are hospitalized for one day after the administration of arsphenamine and rest during the remainder of the week, are better than the results obtained in urban practice, in which the patients are working and cannot be hospitalized. A physician working in a marine hospital stated that the best therapeutic results he had ever seen were in hospitalized syphiltic patients.

In table 3 is shown the ratio of the percentage of patients who gained to that of patients who lost weight. It can be readily seen from this that the ratio between the percentage of patients who gained and the

percentage who lost weight is favorable to the former in the rest plus and rest normal patients of groups I and II, while it reverses sharply in the rest minus patients. (The loss of weight in 100 per cent of the patients of group III is easily explained by the aforementioned forms of disease in the rest plus patients of this group.)

We gained through this study an insight into the habits and ways of living of the average American in Chicago, and the most striking fact gathered seemed to us the scarcity of regular yearly vacations. Only 38 per cent of our patients took vacations. Moreover, the average vacation is one or two weeks, a time insufficient for full relaxation, even if the time is spent as it should be, in a lake cottage or on a fishing trip. But, alas, the majority of the patients stated that they spent their week-ends and vacations touring or visiting with friends!

TABLE 3.—*Ratio of Percentage of Patients Who Gained to That of Patients Who Lost Weight*

| Group | Class | Percentage Who: Gained | Lost |
|---|---|---|---|
| I | rest + | 66 | 34 |
| | rest N | 64 | 33 |
| | rest — | 46 | 52 |
| II | rest + | 77 | 13 |
| | rest N | 66 | 34 |
| | rest — | 26 | 74 |
| III | rest + | 0 | 100 |
| | rest N | .. | ... |
| | rest — | 0 | 100 |

## CONCLUSIONS

The data gained from this study show sufficient beneficial effect of regular and restful living to warrant the statement that the physician who treats syphilis should emphasize to every patient under his care the paramount necessity of rest and relaxation for obtaining the most satisfactory results from antisyphilitic treatment. Failure to observe regular hours of rest and to take vacations leads to poorer results from therapy. Life in the large cities has led to overactivity and frustration of the human need for emotional and physical relaxation. Reeducation to a more restful way of living should be part of the task of physicians.

## SUMMARY

The factors which lead to the general beneficial effect of antisyphilitic treatment are discussed. The seemingly forgotten effect of nonspecific treatment is stressed on the ground of the striking parallels

between syphilitic and tuberculous infection. The value of generalized ultraviolet irradiation and of autohemic injections in certain cases of resistant syphilis is confirmed.

The study deals with the influence of the patient's habits and ways of living on the general beneficial effect derived from therapy. Data compiled by means of questionnaires, analyzed and given in tables, reveal the paramount beneficial influence of restful living on the subjective feeling of well-being as well as on increase of weight on the part of syphilitic patients.

Physicians who treat syphilis should not treat the patient merely specifically but should utilize the value of decreased tension of the patient's life.

# LYMPHOGRANULOMA INGUINALE

## III. THE USE OF LYMPHOGRANULOMATOUS MOUSE BRAINS FOR DIAGNOSIS

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In previous communications [1] we have described the isolation of the virus of lymphogranuloma inguinale from the pus and glandular tissue of a patient with the inguinal type of the disease and its successive transmission through white mice. We have also found, confirming Wassen's [2] observations, that lymphogranulomatous mouse brains offer an excellent source of highly potent and specific antigen for the performance of the Frei test. This work has been repeated recently by Lichtenstein and von Haam.[3]

The purpose of the present paper is to record the results of one year's clinical use of antigen prepared from mouse brain for the diagnosis of lymphogranuloma inguinale. Prior to the introduction of material from experimental animals the only antigen available was that prepared from pus from a human being, as first described by Frei.[4] This original antigen consisted of an emulsion in a physiologic solution of sodium chloride of pus taken from a suppurating gland of a patient with the inguinal type of the disease and heated to destroy the etiologic agent present.

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1. Grace, A. W., and Suskind, F. H.: (*a*) Successive Transmission of Virus of Lymphogranuloma Inguinale Through White Mice, Proc. Soc. Exper. Biol. & Med. **32**:71 (Oct.) 1934; (*b*) Lymphogranuloma Inguinale: II. The Cultivation of the Virus in Mice and Its Use in the Preparation of Frei Antigen, Arch. Dermat. & Syph. **33**:853 (May) 1936.

2. Wassen, E.: Réceptivité de la souris blanche à l'égard du virus lymphogranulomateux (maladie de Nicolas et Favre), Compt. rend. Soc. de biol. **114**:493, 1933.

3. Lichtenstein, L., and von Haam, E.: Usefulness of Organ Emulsions of Infected Animals in Diagnosis of Lymphogranuloma Inguinale, Proc. Soc. Exper. Biol. & Med. **32**:952 (March) 1935.

4. Frei, W.: Eine neue Hautreaktion bei Lymphogranuloma inguinale, Klin. Wchnschr. **4**:2148 (Nov. 5) 1925.

The use of pus from a human subject for the preparation of antigen has several drawbacks, namely:

1. Patients with the inguinal type of lymphogranuloma inguinale in a suppurative stage are not encountered often and can be used as a source of antigen only if the pus is uncontaminated with other organisms. Secondary infection following sinus formation occurs frequently enough to make suitable pus scarce.

2. It is difficult to be certain that pus from inguinal glands is free from the causative agents of other venereal diseases. This applies especially to chancroid, the etiologic agent of which (Ducrey's bacillus) is sometimes found in inguinal pus but is relatively difficult to demonstrate in direct smears or by growth on artificial mediums. The Ito-Reenstierna test with a stabilized vaccine of Ducrey's bacillus enables the determination of a past or present chancroid infection to be made with certainty, but the vaccine required is not readily available.[4a]

3. When a patient from whom suitable pus may be obtained presents himself, the pus is usually available only in small quantities. Only on rare occasions have we been able to aspirate more than from 3 to 5 cc. at one time.

4. Specimens of pus taken from different patients with lymphogranuloma inguinale vary in antigen content.[5] This variation may be so marked that an antigen prepared from a 1:10 dilution of one sample of pus may evoke a strongly positive reaction in a lymphogranulomatous person whereas one made from a 1:5 dilution of pus from another patient may elicit a much weaker reaction in the same subject.

In May 1934, antigen prepared from lymphogranulomatous mouse brain was used for the first time at the New York Hospital for the performance of Frei tests. After a thorough trial of its potency and specificity as compared with antigen prepared from pus from a human being, it has now entirely replaced the latter in the diagnosis of lymphogranuloma inguinale at the New York Hospital.

The clinical conditions which are regarded as manifestations of lymphogranuloma inguinale and which therefore call for the performance of the Frei test are:

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4a. The vaccine used for this test is known as Dmelcos vaccine and is manufactured in France. There is no evidence that the United States Treasury Department has licensed the importation and sale of this vaccine in the United States.

5. (*a*) Grace, A. W.: Lymphogranuloma Inguinale: I. Preservation of Frei Antigen by Drying; Its Concentration in Fresh and Dried Pus, Arch. Dermat. & Syph. **30**:823 (Dec.) 1934. (*b*) Saenz, B.: An Unusual Form of Allergic Cutaneous Reactions in Lymphogranulomatosis Inguinalis, Arch. Dermat. & Syph. **31**:348 (March) 1935.

1. Acute and chronic inguinal adenitis, suppurative or nonsuppurative, in which no other etiologic agent (Gonococcus, Ducrey's bacillus, Spirochaeta pallida, Bacillus tuberculosis, Bacillus tularensis or a simple pyogenic organism) or condition (Hodgkin's disease or neoplasm) can be found. These conditions represent the inguinal type of the disease, which has been described in detail by Durand, Nicolas and Favre,[6] Hellerström,[7] DeWolf and Van Cleve,[8] Cole[9] and many others. It is enough to say here that the untreated condition is chronic and that indolent suppuration of the inguinal glands, sometimes preceded by an evanescent lesion of the genitalia and attended by the formation of multiple sinuses and a violaceous tint of the surrounding skin, should be regarded as suspicious of lymphogranuloma inguinale.

Since mixed venereal infections often occur, it is sometimes advisable to perform a Frei test even if etiologic agents other than that of lymphogranuloma inguinale can be demonstrated in association with inguinal adenitis. This is especially true in instances in which the picture of the bubo is atypical from either a clinical or a pathologic aspect.

2. Acute and chronic inflammatory disease of the anus, rectum and sigmoid colon, which may be accompanied by fistula in ano, rectovaginal fistula, abscesses or sinuses in the buttocks or stricture of the rectum. The condition is independent of the presence or absence of syphilis and gonorrhea. It is referred to as the anorectal type of lymphogranuloma inguinale. Good clinical descriptions of this condition, including esthiomene, have been given recently by Cole,[9] Bloom,[10] Wien and Perlstein[11] and Wien, Perlstein and Neiman.[12]

The commonest symptoms are the passage of blood and pus from the rectum and painful and difficult defecation. Externally, erythema, edema and tenderness of the perianal region or perianal warty excrescences may be found. In most of our patients, however, external lesions

6. Durand, M.; Nicolas, J., and Favre, M.: Lymphogranulomatose inguinale subaiguë d'origine génitale probable, peut-être vénérienne, Bull. et mém. Soc. méd. d. hôp. de Paris **35**:274, 1913.

7. Hellerström, S.: A Contribution to the Knowledge of Lymphogranuloma Inguinale, Acta dermat.-venereol., supp. 1, 1929, p. 5.

8. DeWolf, H. F., and Van Cleve, J. V.: Lymphogranuloma Inguinale, J. A. M. A. **99**:1065 (Sept. 24) 1932.

9. Cole, H. N.: Lymphogranuloma Inguinale, the Fourth Venereal Disease: Its Relation to Stricture of the Rectum, J. A. M. A. **101**:1069 (Sept. 30) 1933.

10. Bloom, David: Stricture of the Rectum Due to Lymphogranuloma Inguinale, Surg., Gynec. & Obst. **58**:827 (May) 1934.

11. Wien, M. S., and Perlstein, M. O.: Lymphogranuloma Inguinale, M. Rec. **139**:288, 1934.

12. Wien, M. S.; Perlstein, M. O., and Neiman, B. H.: Inguinal Lymphogranuloma in Its Relation to Stricture of the Rectum, Arch. Path. **19**:331 (March) 1935.

were rare. Proctoscopic examination may reveal the rectal mucosa to be acutely inflamed and edematous, diffusely and irregularly scarred and ulcerated or converted into a firm, rigid tube. When edema, inflammation or ulceration is present, small nodular elevations of the mucosa are frequent; when it is acute, blood and pus often can be seen passing down the rectum. All degrees of narrowing of the rectal lumen are encountered, varying from that due to edema in the acute condition to a complete stenosis due to fibrosis when the involvement is of long standing. The vast majority of strictures occur between 2 and 6 cm. above the anus, but sometimes they are found as high as 10 cm. Fistulas, with passage of material from the bowel through the vagina or the tissues of the buttocks or thighs, occasionally occur. Pyrexia, as a rule, is not a feature, but instances are occasionally met with in which there is a daily remittent fever, which may last for weeks. Inguinal lymphadenopathy is usually confined to a few shotlike glands. The pathologic picture of anorectal lymphogranuloma inguinale has been given by Barthels and Biberstein [13] and more recently by Wien, Perlstein and Neiman.[12] It is sufficient to state here that the normal tissue of the rectal wall is replaced in the early stages by an unusual type of granulation tissue and in the later stages by hyalinized fibrous tissue. It is this formation of fibrous tissue which is responsible for the resistance of the rectal lesions to therapy in the later stages of the disease. In the early stages the anorectal type of lymphogranuloma inguinale is benefited by the use of antimonial preparations, such as antimony and potassium tartrate, fuadin and stibamine glucoside. Our own cases, as well as those of Hebb,[14] attest this. Investigation of the efficacy of Frei antigen in the treatment of anorectal lymphogranuloma inguinale is now in progress.

Lymphogranuloma inguinale of the anorectal type is said to be most prevalent among women, especially Negroes, and it is probable that most instances of inflammatory rectal stricture in Negro women are due to this disease. It must not be overlooked, however, that similar instances occur in white persons, men as well as women. In the department of dermatology of the New York Hospital, of which the clientele is predominantly white, nine white men and four white women are receiving treatment for this condition at the time of writing.

3. Chronic elephantiasis and ulceration of the vulva (esthiomene). Only one case of this condition has been encountered at the New York Hospital; an adequate description, therefore, cannot be given. Stannus,[15]

13. Barthels, C., and Biberstein, H.: Zur Aetiologie der entzündlichen Rektumstrikturen, Beitr. z. klin. Chir. **152**:161, 325 and 464, 1931.

14. Hebb, Arthur: Personal communication to the authors.

15. Stannus, Hugh S.: A Sixth Venereal Disease, London, Baillière, Tindall & Cox, 1933, p. 125.

in his excellent review on lymphogranuloma inguinale, summarized the symptomatology of esthiomene in the words of Koch:[16]

> The labia majora were the seat of more or less marked thickening, with ulceration, occasionally with angiectatic erosions; rather less commonly the labia minora and clitoris were affected, the latter having often a "stalked" appearance; the skin had a bluish-red color and was ulcerated; sometimes also the mons, the commissure and peri-anal region were involved in the infiltrative process. The epithelium of the nymphae was in some cases smooth and macerated; in others the lips presented a verrucose, tuberose or papillomatous appearance. There was a diffuse sclerotic condition of the mucous membrane about the openings of the urethra and vagina, in some cases leading to definite stricture. Ulceration might occur in any part of these infiltrated tissues, but was most common at the commissure, the opening of the urethra, on the inner surface of the labia minora and clitoris. Perforation might occur of the nymphae, at the fourchette or of the urethrovaginal and rectovaginal walls, with the formation of fistulas; or there might be greater destruction of tissues with the production of a cloaca, limited by portions of infiltrated skin and mucous membranes; rectovesical fistula might also be produced.

Esthiomene and the anorectal conditions previously mentioned constitute the genito-anorectal syndrome described by Jersild[17] and shown to yield a positive Frei reaction by Frei and Koppel.[18]

4. Elephantiasis of the male genitalia. This condition has not yet been encountered at the New York Hospital. Barthels and Biberstein[13] cited the report of a case of elephantiasis of the penis and scrotum occurring nine years after complete extirpation of an involved inguinal gland, which was associated with a typical primary lymphogranulomatous penile lesion. The male genitalia may also show a clinical condition similar to esthiomene in the female.

## METHODS AND MATERIALS

*The Technic of the Frei Test.*—The Frei test, as originally described by Frei,[4] consists of the inoculation into the skin of the flexor surface of the arm of 0.1 cc. of antigen prepared from pus from a lymphogranulomatous inguinal gland diluted 1:10 in a physiologic solution of sodium chloride and heated at 60 C. for two hours on one day and at the same temperature for one hour the next day. Frei discovered that at the end of from forty-eight to seventy-two hours, in a person who has, or has had, lymphogranuloma inguinale, there develops at the site of the injection a bright red papule from 7 to 10 mm. in diameter, whereas a nonlymphogranulomatous subject shows practically no reaction.

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16. Koch, F.: Ulcus vulvae chronicum elephantiasicum, Arch. f. Dermat. u. Syph. **34**:205, 1896.

17. Jersild, O.: Contribution à l'étude de la pathogénie du soi-disant syphilôme ano-rectal (Fournier), Ann. de dermat. et syph. **1**:62, 1920.

18. Frei, W., and Koppel, A.: Ulcus vulvae chronicum elephantiasicum (esthiomène) und sogenanntes syphilôme anorectal als Folgeerscheinungen und der Lymphogranulomatosis inguinalis, Klin. Wchnschr. **7**:2331, 1928.

*The Use of Lymphogranulomatous Mouse Brains in the Frei Test.*—The antigens prepared from mouse brains which were employed in this work were prepared as follows: A mouse dying as a result of a previous intracerebral inoculation with the virus of lymphogranuloma inguinale was killed, and its brain was removed aseptically. The brain was emulsified in a sterile mortar with sterile physiologic solution of sodium chloride, and the emulsion was sealed in glass ampules and heated according to the method of Frei. The increase in virulence of the virus with successive passages in mice and a concurrent increase in the antigen content of mouse brains made it necessary to increase at intervals the dilution of the antigen. Thus, antigens prepared from the brains of mice used for the first to the eleventh passage consisted of a 40 per cent emulsion of mouse brain; those prepared from the brains of mice used for the twelfth to the twenty-third passage consisted of a 20 per cent emulsion, and those prepared from the brains of mice used for the twenty-fourth and subsequent passages consisted of a 10 per cent emulsion; the addition of 0.4 per cent of phenol to the emulsion produced no apparent alteration in its antigenic properties. The antigens were tested for bacterial contamination by aerobic and anaerobic culture before and after heating. Any material that showed bacterial contamination in forty-eight hours was discarded. After heating they were transferred to small vials capped with no-air rubber stoppers and were placed in the refrigerator until used. All antigens were tested within one month after preparation, and several were tested after standing for various lengths of time. It was also found possible to preserve lymphogranulomatous mouse brains by drying them in vacuo from the frozen state according to a method described in a previous communication[5a] and employing that dried material for the production of Frei antigen.

As the antigens increased in potency, it was not only sufficient to increase the dilution but was also necessary to decrease the dose administered for the Frei test. The volume of intradermal inoculum was maintained at 0.1 cc. for antigens prepared from the brains of mice used for the first eleven passages, after which 0.05 cc. was constantly used. To eliminate the possibility of mistaking a pseudoreaction produced by the protein of the mouse brain for a positive Frei reaction, control tests were made concurrently with an emulsion of normal mouse brain prepared and used in the same manner as the antigen prepared from lymphogranulomatous mouse brain.

*Subjects Used for the Performance of the Frei Test with Antigens Prepared from Mouse Brains.*—The series of subjects tested included twenty-seven lymphogranulomatous and thirty-eight nonlymphogranulomatous persons.

Lymphogranulomatous Subjects: The series of lymphogranulomatous patients was made up of two groups: (1) those who presented the inguinal type of the disease and (2) those who showed the anorectal type.

The patients with the inguinal type consisted of twelve men, eleven white and one Negro. Four of them were tested during the active stage of the disease, and the remaining eight, who included the Negro, had healed lesions. Five of the latter had been treated at the New York Hospital within the last two years for purulent inguinal adenitis due to lymphogranuloma inguinale. The three other men had acquired their infections eight, eighteen and twenty years before, respectively, and the condition was recognized by old inguinal scars.

The patients with the anorectal type comprised seven white men and eight women, three white and five Negro. The fifteen patients presented the following lesions: Three patients had acute proctitis, one with an accompanying pyrexia; eight had subacute proctitis with partial rectal stricture, and four had complete stenosis of the rectum, for which colostomy had been performed. The cause of

the rectal condition in three of the patients with colostomy was unknown at the time of operation, which took place from several months to five years prior to admission to the department of dermatology of the New York Hospital. The pathologic report of examination of a portion of the rectal wall removed from one of the women (who also had rectovaginal fistulas) revealed chronically inflamed granulation tissue, with a number of minute round faintly acidophilic bodies, intracellular and extracellular, especially in the more necrotic portions. These bodies closely resembled the intracytoplasmic bodies encountered in lymphogranulomatous inguinal buboes[19] and in the brains of mice which died from infection with the virus of lymphogranuloma inguinale.[20]

Five persons from group 1 and seven from group 2 were syphilitic. Of these twelve patients, three had neurosyphilis, one had a perforated nasal septum and eight had only a positive Wassermann reaction or a history of syphilis.

Nonlymphogranulomatous Subjects: The thirty-eight nonlymphogranulomatous subjects were divided into four groups (groups 3, 4, 5 and 6) as follows:

Group 3 was made up of seven patients who showed inflammatory inguinal adenitis at the time of Frei testing. Four of them had chancroid, as determined by a positive reaction to the Ito-Reenstierna test, two had staphylococcic abscesses and one had primary syphilis. Two members of this group also had latent syphilis.

In group 4 there were four persons with rectal disease. Of these, one had primary rectal syphilis with inguinal buboes and three had neoplasms.

Group 5 consisted of twenty-two inpatients of the general medical and surgical services who had no history of inguinal lymphadenopathy, rectal disease or syphilis.

In group 6 there were seven persons with syphilis, three of whom were also in groups 3 and 4. Of the four not mentioned heretofore, one had dementia paralytica, another had tabes and two had the disease in a latent form.

Owing to the large number of antigens tested, eighty-eight in all, in addition to the control material, and to the limited number of subjects available, each person was given repeated inoculations at intervals, at least two antigens being given at one time. Duplicate and triplicate tests in different lymphogranulomatous and nonlymphogranulomatous subjects were made as often as possible with each antigen. In this way, 150 tests were performed in the twenty-seven lymphogranulomatous subjects and 143 in the thirty-eight nonlymphogranulomatous ones.

## RESULTS

*Reaction to Inoculation with Antigen Prepared from Mouse Brain.*—The results obtained by the use of lymphogranulomatous mouse brains for the diagnosis of lymphogranuloma inguinale are set forth in table 1. The antigens employed were prepared from the brains of mice used for the second to the forty-fourth passage of the virus and were prepared and administered according to the methods given in the preceding section.

It will be noted that in compiling the table only the size of the central papule was recorded and no mention was made of the surrounding erythematous zone, which usually was present at the end of from forty-eight to seventy-two hours,

19. Favre, M.: Sur l'étiologie de la lymphogranulomatose inguinale subaiguë (ulcère vénérien adénogène), Presse méd. **32**:651, 1924.

20. Findlay, G. M.: Experiments on the Transmission of the Virus of Climatic Bubo (Lymphogranuloma Inguinale) to Animals, Tr. Roy. Soc. Trop. Med. & Hyg. **27**:35 (June) 1933. Grace and Suskind.[1b]

especially in positive reactions. The reason for the omission is that the size of the papule was the most constant element of the reaction and the size of the surrounding flare varied considerably. Erythema was seldom observed in negative reactions.

TABLE 1.—*Reactions of Various Groups of Subjects to Tests with Frei Antigen Prepared from Lymphogranulomatous Mouse Brain and with Emulsion of Normal Mouse Brain*

| Material Used in Intradermal Test | Lymphogranulomatous Persons | | | Nonlymphogranulomatous Persons | | |
|---|---|---|---|---|---|---|
| | Average Size of Papule, Mm. | Number of Persons Tested | Number of Tests | Average Size of Papule, Mm. | Number of Persons Tested | Number of Tests |
| (1) All Lymphogranulomatous and Nonlymphogranulomatous Persons | | | | | | |
| Lymphogranulomatous mouse brain | 8.7 | 27 | 95 | 2.7 | 38 | 105 |
| Normal mouse brain | 2.2 | 27 | 55 | 2.0 | 38 | 38 |
| (2) Persons with Active Inflammatory Inguinal Adenitis | | | | | | |
| Lymphogranulomatous mouse brain | 9.0 | 4 | 17 | 3.0 | 7 | 19 |
| Normal mouse brain | 2.1 | 4 | 7 | 2.3 | 7 | 12 |
| (3) Persons with Old Healed Inguinal Lymphogranuloma Inguinale | | | | | | |
| Lymphogranulomatous mouse brain | 9.2 | 8 | 28 | | | |
| Normal mouse brain | 2.6 | 8 | 9 | | | |
| (4) Persons with Rectal Diseases | | | | | | |
| Lymphogranulomatous mouse brain | 8.2 | 15 | 50 | 2.8 | 4 | 9 |
| Normal mouse brain | 2.2 | 15 | 20 | 2.1 | 4 | 4 |
| (5) Persons with Syphilis | | | | | | |
| Lymphogranulomatous mouse brain | 8.9 | 12 | 48 | 2.5 | 7 | 12 |
| Normal mouse brain | 3.1 | 12 | 19 | 1.8 | 7 | 8 |
| (6) Nonlymphogranulomatous Persons Without Inguinal or Rectal Disease or Syphilis | | | | | | |
| Lymphogranulomatous mouse brain | ... | .. | .. | 2.4 | 22 | 56 |
| Normal mouse brain | ... | .. | .. | 1.6 | 22 | 22 |

An analysis of table 1 follows:

All Lymphogranulomatous and Nonlymphogranulomatous Persons: The great difference in reaction to antigen prepared from lymphogranulomatous mouse brain between lymphogranulomatous and nonlymphogranulomatous subjects is apparent, the average diameter of the papule in the former being 8.7 mm. and that in the latter, 2.7 mm. The emulsion of normal mouse brain produced no reaction which could be regarded as positive in any group of subjects, and the reactions obtained therewith approximated the responses to antigen prepared from lymphogranulomatous mouse brain in subjects who had never had the disease.

The papules produced by individual positive reactions ranged from 7 mm. to 30 by 22 mm. in diameter, 77 per cent of them being from 7 to 10 mm. in diameter. The latter figure agrees with that observed by Frei as the average size of the papule in persons with lymphogranuloma inguinale. The upper limit of the size of the papule in negative reactions obtained with material prepared from either normal or infected mouse brain was 5 mm. and was seen in six persons only.

Patients with Inflammatory Inguinal Adenitis and Rectal Disease: That the Frei test as performed with antigen prepared from lymphogranulomatous mouse

brain is specific for lymphogranuloma inguinale is brought out by the data given in parts 2, 4 and 6 of table 1. Subjects with inflammatory inguinal adenitis and rectal disease in whom etiologic agents or conditions other than lymphogranuloma inguinale were demonstrated responded no differently to antigen prepared from lymphogranulomatous mouse brain than did nonlymphogranulomatous persons without inguinal adenitis or rectal disease. Their reactions could in no way be confused with the positive reactions of persons with the active inguinal or rectal type of the disease.

No significant difference was observed between the average size of the papule in positive reactions of patients with active lymphogranuloma inguinale of the inguinal type and that of patients who had recovered from the disease (parts 2 and 3, table 1). The central papule was, on the average, slightly smaller in patients with the anorectal type than in those with the inguinal type, but this difference was no greater than that seen among the various groups of patients with negative responses.

Patients with Syphilis: The presence of active or arrested syphilis had no influence on the reaction to antigens prepared from lymphogranulomatous mouse brains in persons who were or were not at the same time sensitized to the virus of lymphogranuloma inguinale. Lymphogranulomatous persons with syphilis showed on an average a papule 8.9 mm. in diameter, while nonlymphogranulomatous persons with syphilis manifested a 2.5 mm. papule. These figures are presented in parts 5 and 6 of table 1.

*Results of Other Observations.*—Other observations that we have made in this study have included: (1) the quality of positive reactions to antigens prepared from mouse brain as compared with those to antigens prepared from pus from human subjects; (2) the possibility of desensitization to the virus or of sensitization to the virus or to the protein of mouse brain after repeated inoculations of antigen prepared from mouse brain in the same person, and (3) the keeping quality of antigen prepared from mouse brain. These observations will be dealt with in order:

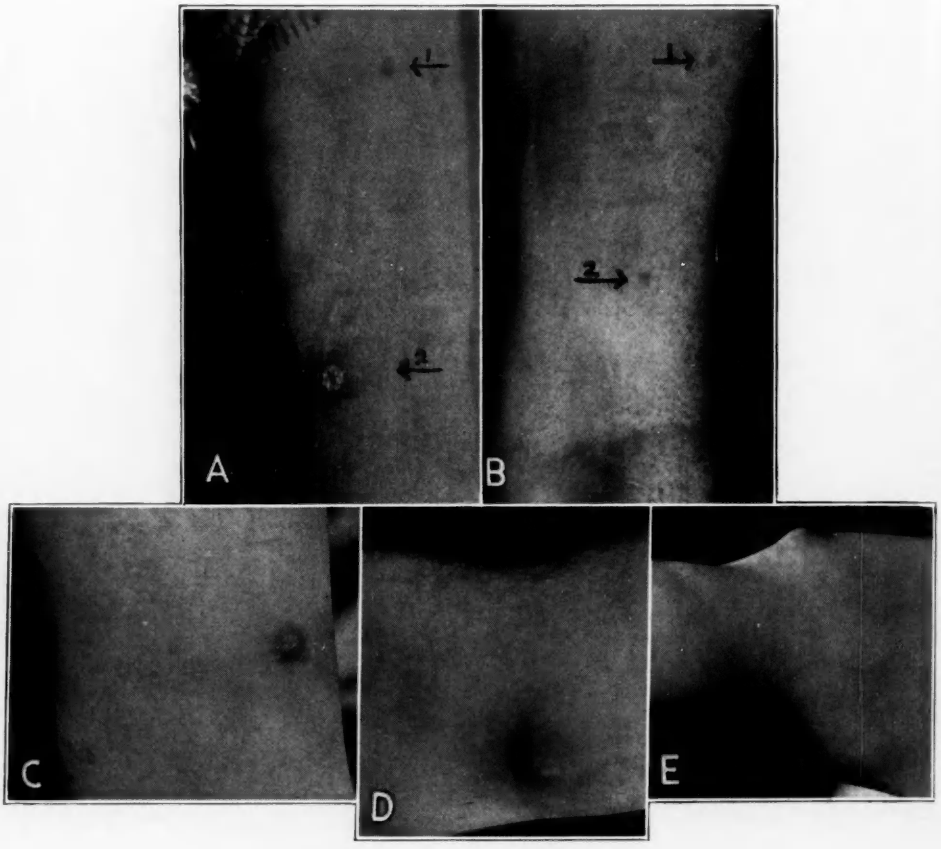
Comparison of Reactions to Antigen Prepared from Mouse Brain and Antigen Prepared from Pus from a Human Subject: The positive reaction to antigen prepared from mouse brain was in most instances qualitatively more intense than the reaction produced by antigen prepared from pus from a human subject. The central papule was higher and more scarlet and was more likely to have a relatively large vesicular or pustular center, which sometimes became necrotic; also, the area of erythema immediately surrounding the papule was usually brighter and more extensive. The reactions generally began to recede by the fourth day, ultimately leaving a slightly pigmented area or a small scar. Infrequently, diffusely papillated erythematous areas about 1 cm. in diameter were encountered instead of a single central papule.

The cause of pustulation in Frei reactions has not been definitely determined. Strauss and Howard [21] on slender evidence expressed the belief that it is due to the incomplete absorption of antigenic material. Our unpublished observations have indicated that it is a manifestation of a strong reaction.

Desensitization of Human Skin Following Repeated Intradermal Inoculations of Antigen Prepared from Mouse Brain: Wien and Perlstein [22] reported tem-

21. Strauss, M., and Howard, M. E.: The Frei Test for Lymphogranuloma Inguinale, J. A. M. A. **103**:1830 (Dec. 15) 1934.

22. Wien, M. S., and Perlstein, M. O.: Intradermal Treatment of Lymphogranuloma Inguinale, Arch. Dermat. & Syph. **28**:42 (July) 1933.




*A*, seventy-two hour reaction to antigens prepared from normal mouse brains and from lymphogranulomatous mouse brains in a patient with active lymphogranuloma inguinale of the inguinal type. *1* indicates the low papule, 4 by 4 mm., produced by inoculation with an emulsion of normal mouse brains. *2* indicates the infiltrated erythematous area, 20 by 20 mm., surmounted by a vesicle 10 by 9 mm., produced by inoculation with antigen prepared from lymphogranulomatous mouse brains. *B*, forty-eight hour reaction to an emulsion of normal mouse brains and to antigen from lymphogranulomatous mouse brains in a nonlymphogranulomatous subject. *1* indicates the low papule, 3 by 4 mm., produced by inoculation with the emulsion of normal mouse brains. *2* indicates the low papule, 4 by 5 mm., produced by inoculation with antigen prepared from lymphogranulomatous mouse brains. *C*, seventy-two hour reaction to antigen prepared from lymphogranulomatous mouse brains in a patient with anorectal lymphogranuloma inguinale. There was an erythematous papule 10 mm. in diameter. The reaction to an emulsion of normal mouse brains in this subject was a 3 by 2 mm. nonerythematous low papule. *D*, seventy-two hour reaction to antigen prepared from lymphogranulomatous mouse brains in a very strong reactor. There was an erythematous papule 30 by 22 mm., rising 7 mm. from the surface of the skin; the center contained a 7 mm. vesicle. The reaction to an emulsion of normal mouse brains in this patient, who presented the anorectal type of the disease, was a nonerythematous low papule 2 by 3 mm. *E*, lateral view of the papule depicted in figure *D*, showing the unusual height of the papule.

porary local desensitization of the skin of a patient to the virus of lymphogranuloma inguinale after repeated intradermal inoculations of Frei antigen prepared from pus from a human being. In our series of cases, ten lymphogranulomatous subjects received five or more intradermal inoculations of antigen prepared from mouse brain at various intervals, and in none did the repetition of the test produce any diminution in the size and quality of the reaction. Practically all these tests were performed on both the upper and the lower part of the arm; four segments of the limb were thus available, and successive tests were seldom performed on the same segment. It is probable that failure to produce local desensitization was due to the long interval which elapsed between successive inoculations of the same segment. The data relating to this series of inoculations are set forth in table 2.

Sensitization of Human Skin to the Protein of Mouse Brain: A review of the reactions to antigen prepared from normal mouse brain in all our subjects showed that none possessed a natural hypersensitivity to the protein of mouse brain. There was, however, the possibility of effecting an acquired hypersensitivity

TABLE 2.—*Intervals Between Successive Inoculations of the Same Segment of the Arm*

| Subject | Type of Lymphogranuloma Infection | Frei Tests | | |
|---|---|---|---|---|
| | | Number Performed | Shortest Interval Between Successive Tests on Same Segment, Days | Interval Between First and Last Tests, Months |
| McG. | Anorectal | 18 | 32 | 10 |
| B. | Anorectal | 16 | 65 | 8 |
| G. | Inguinal | 9 | 16 | 7 |
| J. | Anorectal | 9 | 17 | 10 |
| R. | Anorectal | 9 | 90 | 3 |
| A. | Inguinal | 8 | 5 | 1 |
| L. | Inguinal | 8 | 72 | 5 |
| C. | Inguinal | 7 | 76 | 5 |
| C. | Inguinal | 6 | No repetition on same segment | 4 |
| E. | Inguinal | 5 | 71 | 2 |

by the repeated inoculation with antigen over a period of months. Hence the reactions of all subjects, particularly of those listed in table 2, were studied with this point in mind. One person only (G), after receiving nine tests in a period of seven months, exhibited a somewhat larger papule and a more intense positive response at the end of that time. That this increase was due to an acquired hypersensitivity to the protein of mouse brain was evident from the fact that his concurrent reaction to material prepared from normal mouse brain was a 5 mm. papule with a surrounding flare 40 mm. in diameter. His earlier reactions to normal mouse brain showed only average-sized papules. None of the sixty-four other subjects exhibited a similar phenomenon. It is felt, therefore, that whereas an acquired hypersensitivity to the protein of mouse brain might be produced by the repeated use of the antigen in the same person for diagnosis, it probably occurs infrequently and then is of insufficient degree to produce a false positive result. Not enough inoculations of nonlymphogranulomatous subjects with antigen prepared from lymphogranulomatous mouse brains have been performed to make valid any statement as to the possibility of producing sensitization to the virus.

The Keeping Quality of Antigen Prepared from Mouse Brain: All the antigens were tested in human subjects within one month after preparation, and several were tested as long as eight months later. None had shown any decrease in potency on standing for that length of time.

COMMENT

Antigen prepared from mouse brain infected with the virus of lymphogranuloma inguinale can replace that prepared from pus from a human being for the performance of the Frei test. This statement is based on the results of 95 tests on twenty-seven lymphogranulomatous persons and of 105 tests on thirty-eight nonlymphogranulomatous persons. Eighty-eight different specimens of antigen were used, which were prepared from the brains of mice used for the second to the forty-fourth passage of a single strain of the virus. The tests were carried out over a period of one year. By proper dilution of antigen prepared from mouse brain it was possible to obtain results which agreed closely with those obtained by the use of antigen prepared from pus from a human being. The average diameter of the papule in a positive reaction was 8.7 mm., and that in a negative reaction, 2.7 mm. The sensitivity of the antigen prepared from mouse brain was as high as that of the most potent antigens prepared from pus from our patients. No instance was found in which the cutaneous effect of the protein of the mouse brain could be regarded as producing a false positive reaction. Earlier in this paper it was pointed out that one of the chief disadvantages of antigen prepared from pus from a human subject is the possibility of the presence in the pus of other organisms which are difficult to demonstrate. Antigen prepared from mouse brain has not this disadvantage. Mice, however, suffer from spontaneous encephalitis of virus origin [23] and can harbor the virus of choriomeningitis without showing any sign of its presence. The latter virus has been studied by Traub [24] and Armstrong [25] and has been shown by Rivers [26] to be identical with the causative agent of a form of meningitis in man. Infectious ectromelia of mice [27] need not be considered here.

During the course of this work we have been aware of the possibility of the coexistence of a virus disease like that of Theiler,[23] Armstrong,[25] and Traub,[24] along with our strain of the virus of lymphogranuloma inguinale. Such a virus could have been latent in our stock mice and picked up some time during intracerebral passage of the virus of lymphogranuloma inguinale or could have been obtained from the original

23. Theiler, Max: Spontaneous Encephalitis of Mice: A New Virus Disease, Science **80**:122 (Aug. 3) 1934.

24. Traub, E.: A Filterable Virus Recovered from White Mice, Science **81**: 298 (March 22) 1935.

25. Armstrong, C., and Lillie, R. D.: Experimental Lymphocytic Choriomeningitis of Monkeys and Mice Produced by a Virus Encountered in Studies of the 1933 St. Louis Encephalitis Epidemic, Pub. Health Rep. **49**:1019 (Aug 31) 1934.

26. Rivers, T. M., and Scott, T. F. McNair: Meningitis in Man Caused by a Filterable Virus, Science **81**:439 (May 3) 1935.

27. Marchal, J.: Infectious Ectromelia, J. Path. & Bact. **23**:713, 1930.

human inoculums. We have examined our material carefully with this point in mind and shall describe our observations under the two following headings:

*Experiments with Normal Stock Mice (Rockland Farms).*—Following the technic of Traub,[24] 200 stock mice were inoculated with 0.03 cc. of sterile broth intracerebrally in an attempt to activate a latent infection. Only negative results were obtained. Also, in connection with our experiments on the transmission of the virus of lymphogranuloma inguinale, in no instance were there observed any signs of illness in the control animals which received intracerebral inoculations of a physiologic solution of sodium chloride, Tyrode's solution, ascitic fluid, broth of $p_H$ 8, heated emulsion of infected mouse brain or emulsion of normal mouse brain.

*Observations on Mice Inoculated with the Virus of Lymphogranuloma Inguinale.*—The signs observed in these animals were the same in each generation and much like the signs reported by other investigators. There was nothing to indicate the presence of any unusual element in the condition. Traub[28] has also recently carried out cross-immunity and cross-neutralization experiments with our strain of the virus of lymphogranuloma inguinale and the virus of choriomeningitis and has shown the two viruses to be immunologically distinct.

We feel, therefore, that the antigens prepared from mouse brains used in this work contained no other virus than that of lymphogranuloma inguinale. We are of the opinion, also, that the likelihood of introducing an extraneous virus is negligible provided that mice of the same clean stock obtained from a single reliable breeder are always used and that these mice are tested periodically for the presence of latent virus disease.

## SUMMARY

It has been found that Frei antigen can be prepared from the brain of a mouse infected with the virus of lymphogranuloma inguinale.

The original Frei antigen as prepared from pus from a human being has many drawbacks.

There are at least four distinct conditions due to lymphogranuloma inguinale which may be diagnosed by the performance of the Frei test.

Antigen prepared from mouse brain has been tried for one year at the New York Hospital for the diagnosis of lymphogranuloma inguinale. The preparation and administration of eighty-eight different specimens of antigen, derived from the brains of mice used for the second to the forty-fourth passage of a single strain of virus, and the results of their use in twenty-seven patients with the disease and in thirty-eight nonlymphogranulomatous subjects are described in detail.

The average positive reaction to antigen prepared from mouse brain was an erythematous papule 8.7 mm. in diameter, with a surrounding flare of varying size; 77 per cent of these reactions showed a central papule from 7 to 10 mm. in diameter.

28. Traub, E.: Personal communication to the authors.

No reaction which could be regarded as positive was obtained in any person by the use of antigen prepared from lymphogranulomatous mouse brain in nonlymphogranulomatous persons or by the use of emulsions of normal mouse brain, prepared in the same way as the antigen.

The results of tests on patients with conditions which must be differentiated from lymphogranuloma inguinale were definitely negative.

The presence of active or arrested syphilis had no effect on the reaction to the Frei test performed with antigen prepared from mouse brain.

By standardization of dilution and dosage it was possible to produce reactions quantitatively the same as those to antigens prepared from human pus; qualitatively, however, the reactions were usually more intense.

No desensitization of the skin of any lymphogranulomatous subject was observed after repeated inoculations with antigen prepared from mouse brain. Low grade sensitization to the protein of mouse brain, however, was seen in one instance.

Antigen prepared from mouse brain has been found to retain its potency for at least eight months after preparation.

Experiments have been performed to detect the coexistence of spontaneous virus disease of mice with our strain of the virus of lymphogranuloma inguinale. Only negative results have been obtained.

It is felt, therefore, that antigen prepared from lymphogranulomatous mouse brain can replace that prepared from pus from a human being for the diagnosis of lymphogranuloma inguinale. Not only is it as sensitive and specific as the most potent antigen prepared from human material, but it overcomes the disadvantages of the latter.

# STUDIES IN THE GENUS MICROSPORUM

## II. BIOMETRIC STUDIES

NORMAN F. CONANT, PH.D.

DURHAM, N. C.

Attempts to present the morphologic characters of the dermatophytes for the purpose of making their identification easier have not resulted in a classification which clearly distinguishes the specific characters. In this respect, Ota and Langeron [1] defined genera but merely listed the species which they considered should be included in these genera. Likewise, Grigorakis,[2] although he treated specific characters more thoroughly than the previous authors, failed to present a diagnostic key to the species studied, as he became involved in the theoretical rôle of pleomorphism among these forms.

Other attempts to classify the dermatophytes mycologically have resulted in a discussion of their possible relationship to the Gymnoascaceae. In this respect, Matruchot and Dassonville,[3] Nannizzi [4] and Langeron and Milochevitch [5] have in turn compared the morphologic similarities of the two groups and have proposed a classification in which the dermatophytes have been included among the Gymnoascaceae. To make such a classification effective, the ascospore stage in the life cycle of the dermatophytes should be found, and the similarity of this stage to that of the Gymnoascaceae should be proved. Nannizzi [6] attempted

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Contribution 140 from the Laboratory of Cryptogamic Botany and the Farlow Herbarium, Harvard University.

1. Ota, M., and Langeron, M.: Nouvelle classification des dermatophytes, Ann. de parasitol. **1**:305, 1923.

2. Grigorakis, L.: Recherches cytologiques et taxonomiques sur les dermatophytes, Ann. d. sc. nat. bot. **7**:165, 1925.

3. Matruchot, L., and Dassonville, C.: Sur le champignon de l'herpes et les formes voisines et sur la classification des ascomycètes, Bull. Soc. mycol. de France **15**:240, 1899; Sur le Ctenomyces serratus Eidam comparé aux champignons des teignes, ibid. **15**:305, 1899; Sur une forme de reproduction d'ordre élevé chez le trichophyton, ibid. **16**:201, 1900.

4. Nannizzi, A.: Ricerche sui rapporti morfologici tra Gymnoascaceae e Dermatomiceti, Ann. mycol. **24**:85, 1926.

5. Langeron, M., and Milochevitch, S.: Morphologie des dermatophytes sur milieux naturels et milieux à base de polysaccharides: Essai de classification, Ann. de parasitol. **8**:465, 1930.

6. Nannizzi, A.: Ricerche sull' origine saprofitica dei funghi delle tigne: II. Gymnoascus gypseus sp. n. forma ascofora del Sabouraudites (Achorion) gypseus (Bodin) Ota and Langeron, Atti d. r. Accad. d. fisiocrit. in Siena **2**:89, 1927.

to do this when he reported the finding of ascospores in Achorion gypseum. Tate,[7] however, could not confirm this report, nor have others been able to do so. It therefore appears to me that, since ascospores are not produced and the fungi therefore cannot be described with regard to these stages, it is more desirable to base the classification of the dermatophytes on structures which are found, namely, the imperfect asexual spore forms.

Among the fungi imperfecti certain groups have been studied and classified on the basis of the type and character of the spores produced, the manner in which they are borne and the arrangement and character of their supporting structures. Such studies have resulted in a usable classification of this group of fungi. I have therefore studied species of the genus Microsporum for the purpose of presenting diagnostic characters which will enable identification of cultures.

## MORPHOLOGY OF THE GENUS MICROSPORUM

That the dermatophytes differ in their type of growth and ability to produce spore forms on various artificial mediums has been pointed out several times. Because of this, Grigorakis [2] studied only "mother cultures," or primary isolations. When this method is used he expressed the belief that the characters first presented on culture are the true characters of the fungi, whereas in subsequent transfers the spore forms and other features are lost. This loss of distinguishing spore forms has greatly hindered prolonged morphologic studies of the fungi of the skin in many instances. It has been found, however, that in many cases the fungi do not produce characteristic spore types when first cultured. Davidson, Dowding and Buller [8] have shown that spores have been produced in some of their cultures only after several transfers. I have also found that a great many cultures do not at first produce the spore types of the genus Microsporum.

It was necessary, therefore, to secure a consistent growth of species of Microsporum in culture before a detailed study of the spore forms and attendant mycelial characters could be used for specific differentiation. With this in mind I [9] studied several cultures and found that a consistent production of spore forms in the genus Microsporum could be induced in rice cultures. On this medium the heavily sporulating mats of mycelium readily yielded material for study.

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7. Tate, P.: The Dermatophytes or the Ringworm Fungi, Biol. Rev. **4**:41, 1929.

8. Davidson, A. M.; Dowding, E. S., and Buller, A. H. R.: Hyphal Fusions in Dermatophytes, Canad. J. Research **6**:1, 1932.

9. Conant, N. F.: Studies in the Genus Microsporum: I. Cultural Studies, Arch. Dermat. & Syph. **33**:665 (April) 1936.

In rice cultures the most characteristic spore form produced was the long, tapering, spindle-shaped multicellular spore called a fuseau (fig. 1, *1*). This large spore, or macroconidium, appeared terminally on the aerial hyphae, whereas the small single-cell spores, the aleuries or microconidia (fig. 1, *3*), were borne laterally along the hyphae. Also in the aerial hyphae and in cultures grown on the "natural mediums" of Langeron and Milochevitch,[5] were long slender spirals (fig. 1, *2*). These spirals are characteristic of a great many fungi of the genus Trichophyton. In the mycelial mat were seen chlamydospores (fig. 1, *7*), the large thick-walled resting spores, raquet hyphae (fig. 1, *6*) with enlarged, swollen distal ends and pectinate hyphae (fig. 1, *5*), which were short comblike formations with projections on the curved periphery. In addition to these bodies which occurred regularly, a structure seen in many of the Microspora was the so-called nodular

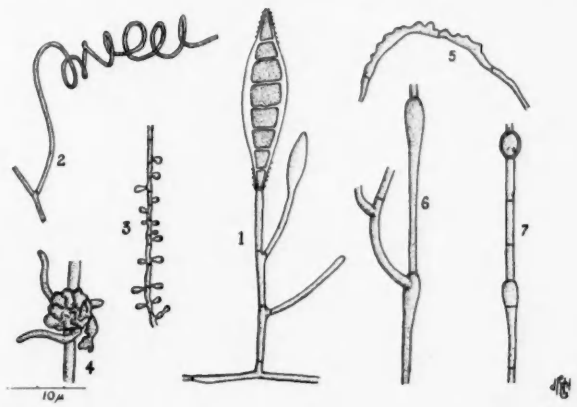


Fig. 1.—Representative structures in the genus Microsporum: *1*, mature macroconidium (fuseau) seen in optical section (the immature macroconidium begins as a swelling at the apex of the side branch); *2*, spiral hypha; *3*, laterally borne microconidia; *4*, nodular body; *5*, pectinate hypha; *6*, raquet hypha; *7*, chlamydospore, a thick-walled resting spore.

body (fig. 1, *4*). This structure was the result of the intertwining and knotting of mycelial branches either from the same hyphal strand or from those adjacent. At times this body was represented only by a coiling of one hyphal strand around another, and hence by some investigators this structure has been thought to bear some resemblance to the ascogonial coil found in the Ascomycetes. However, it has never been seen to mature into an ascus-producing body.

### COMPARISON OF MACROCONIDIA IN THE GENUS MICROSPORUM

Since the macroconidium (fuseau) is the most important spore form of the genus Microsporum, its value as a diagnostic specific character

must be established if a usable taxonomic treatment of the genus is to be based on it. Distinctive characters of the spores, such as the size, shape, color and thickness of the wall, the nature of the surface of the wall (whether smooth or echinulate), the septations and the manner in which the spores are borne from their supporting structures must be taken into consideration in an effort to find specific differences. While searching for these characters in a number of cultures, I was impressed with the great variation in length and width and in the number of septations seen in macroconidia from the same culture. Such a condition, however, is present not only in the genus Microsporum but in other members of the group of fungi imperfecti.

In view of a plasticity of diagnostic structures in other groups of fungi, they have been studied to determine the degree of variation and the means by which the variation may best be expressed. For this purpose, biometric studies of the types of reproductive bodies observed in culture or elsewhere have been resorted to in order to group or to distinguish forms which appear too closely related for satisfactory separation otherwise. In this way, Rosenbaum [10] and Tucker [11] studied the genus Phytophthora and Braun [12] the genus Pythium. In the rusts Stakman and Piemeisel,[13] Stakman and Levine [14] and Levine [15] found that physiologic forms could be identified on the basis of their morphology if measurements were taken from material grown under favorable conditions and on congenial hosts. In the fungi imperfecti, to which the dermatophytes belong, the same type of study has been applied to Helminthosporium. In this genus the large septate spores are not unlike those of Microsporum. By means of a biometric study (length, width and number of septations) of the conidia of two species

10. Rosenbaum, J.: Studies of the Genus Phytophthora, J. Agric. Research **8**:233, 1917.

11. Tucker, C. M.: Taxonomy of the Genus Phytophthora de Bary, Research Bulletin 153, Agric. Exper. Stat., University of Missouri, 1931.

12. Braun, H.: Comparative Studies of Pythium debaryanum and Two Related Species from Geranium, J. Agric. Research **30**:1043, 1925.

13. Stakman, E. C., and Piemeisel, F. J.: Biologic Forms of Puccinia graminis on Cereals and Grasses, J. Agric. Research **10**:429, 1917.

14. Stakman, E. C., and Levine, M. N.: Effect of Certain Ecological Factors on the Morphology of Urediospores of Puccinia graminis, J. Agric. Research **16**:43, 1919.

15. Levine, M. N.: A Statistical Study of the Comparative Morphology of Biologic Forms of Puccinia graminis, J. Agric. Research **24**:539, 1923. Biometrical Studies of the Variation of Physiologic Forms of Puccinia tritici and the Effects of Ecological Factors on the Susceptibility of Wheat Varieties, Phytopath. **18**:7, 1928.

of Helminthosporium, Nisikado and Miykade [16] found reliable diagnostic differences which had not at first been apparent.

Since such a successful application of biometrics has been made in various other groups of fungi, I have attempted to apply this type of study to Microsporum.

The fungi were grown on polished rice in flasks made up with one part rice to three parts water and sterilized in free steam for one hour on two successive days. Bits of the sporulating mycelium from these flasks were carefully teased apart in lactophenol cotton blue. In these mounts the macroconidia were carefully measured, and curves were plotted for the various species. By the use of these simple curves it was found that the characteristic size of the spores of a given species could be more easily recognized, while at the same time a comparison of the curves would lead to a differentiation of the species.

The cultures studied and the sources from which they were received have been listed elsewhere,[9] and the same groupings will be used in this paper:

Group I. Microsporum fulvum 483,24; Microsporum gypseum 12,12a,13
Group II. Microsporum lanosum 19,27,29,33,486
Microsporum felineum, 5, 481
Group III. Microsporum equinum 50, 485
Group IV. Microsporum obesum 40
Microsporum aurantiacum 43
Microsporum simiae 80
Microsporum pseudolanosum 42

The macroconidia of these cultures seemed to be grouped together into eight categories, based not alone on their size but also on their shape, the thickness of their walls and the amount of roughness. The microscopic aspect of these macroconidia may be seen in figure 2. The spores in this figure demonstrate the degree of variability in the single species as well as the degree of similarity between different species. It will be seen that *A* and *D*, *B* and *E*, and *C* and *F* differ markedly not only in size but in shape and in the amount of roughness. The first six groups may be seen to differ from groups *G* and *H* in size and in the thickness of their walls. However, *A*, *B* and *C* are similar in all respects, as are *D*, *E* and *F*, and *G* and *H*. When such similarities exist, real differences are demonstrated only when great numbers of specimens are considered and a quantitative means of comparison is employed.

Such a means of comparison is that of curves in which the sizes of the spores are plotted against the number of the spores measured. The fungi of group I, M. fulvum and M. gypseum, have the small thin-walled type of macroconidium (fig. 2 *G* and *H*). Macroconidia from six different isolations of these two species were studied and measured to determine if two clearcut species existed. For this purpose 200 macroconidia each of M. gypseum 12, 12a and 13 were compared with a like number of macroconidia of M. fulvum 24, 483 and an additional strain not on the list, M. fulvum N. Y. The curves of the length of the macroconidia of these six isolates are plotted in figure 3. The size interval includes 2 microns; i. e., spores were grouped together which fell within the length of from 28 to 30

16. Nisikado, Y., and Miykade, C.: Studies on Two Helminthosporium Diseases of Maize Caused by H. turcicum Passerini and Ophiobolus heterostrophus Drechsler (= Helm. Maydis Nisikado et Miykade), Ber. Ohara Inst. **3**:221, 1926.

microns, from 30 to 32 microns, and so forth. It will be seen in figure 3 that the three isolations of M. fulvum 24, 483 and N. Y. fall into one group, with peaks at from 38 to 40 microns, while M. gypseum 12, 12a and 13 fall into another group with peaks at from 44 to 46 microns. To bring out these differences more clearly, a regrouping of the count in figure 3 was made so that 600 macroconidia of one group were compared with 600 macroconidia of the other. The curves for this grouping presented in figure 4 indicate two distinct species, M. fulvum having a definite peak at 38 microns and M. gypseum having a definite peak at 44 microns. Such a difference in the two species had not been readily apparent heretofore, as these two species have been considered morphologically identical (Ota and Langeron[1] and Grigorakis[17]). These authors, however, did not reduce either to synonomy but maintained both specific names.

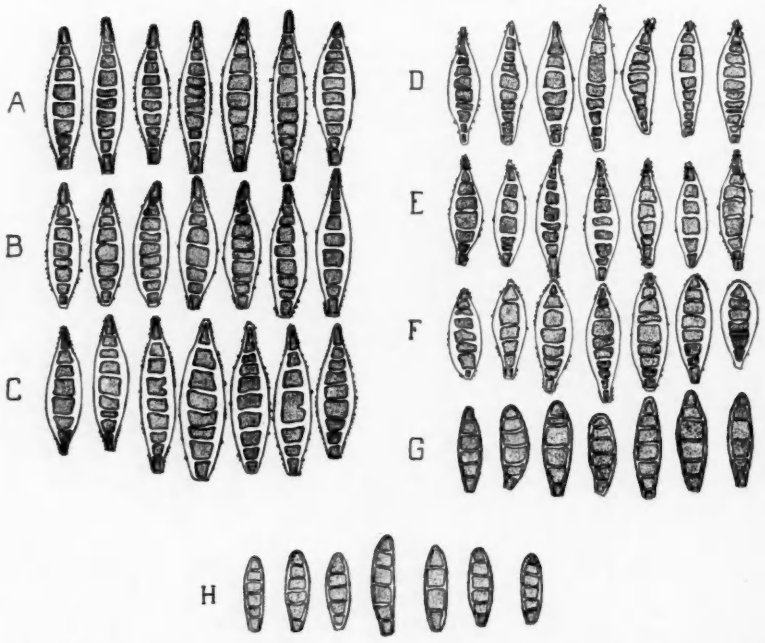


Fig. 2.—Representative macroconidia in eight species of Microsporum, demonstrating the variations in length, width, number of septations and roughness of the walls: *A*, Microsporum lanosum; *B*, Microsporum pseudolanosum; *C*, Microsporum aurantiacum; *D*, Microsporum equinum; *E*, Microsporum simiae; *F*, Microsporum obesum; *G*, Microsporum gypseum; *H*, Microsporum fulvum.

In the same manner the curves of the spores of M. lanosum and M. felineum of group II were compared. In this comparison the curves of the lengths of 200 macroconidia each from four isolations of M. lanosum 486, 19, 27 and 33 and 200 macroconidia from M. felineum 5 are presented in figure 5. It will be seen that the curves of M. lanosum 486, 19 and 27 and M. felineum 5 show a close agreement. The curve for M. lanosum 33, however, attains a peak of 78 microns,

17. Grigorakis: Dermatophytes et dermatomycoses, Ann. de dermat. et syph. **10**:18, 1929; footnote 2.

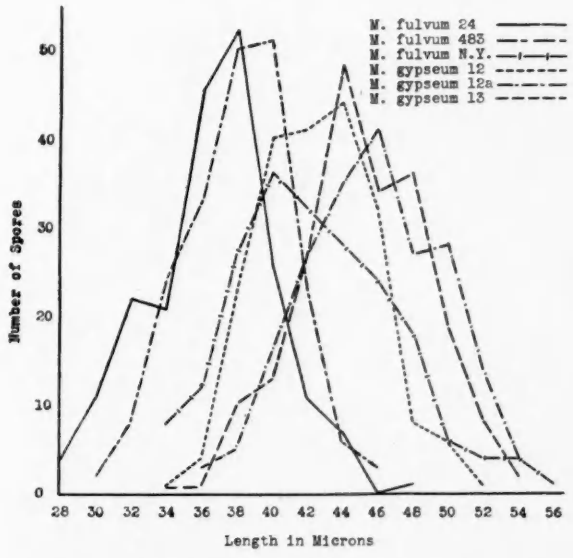


Fig. 3.—Comparison of the lengths of 200 macroconidia each of three isolations of M. fulvum and three of M. gypseum.

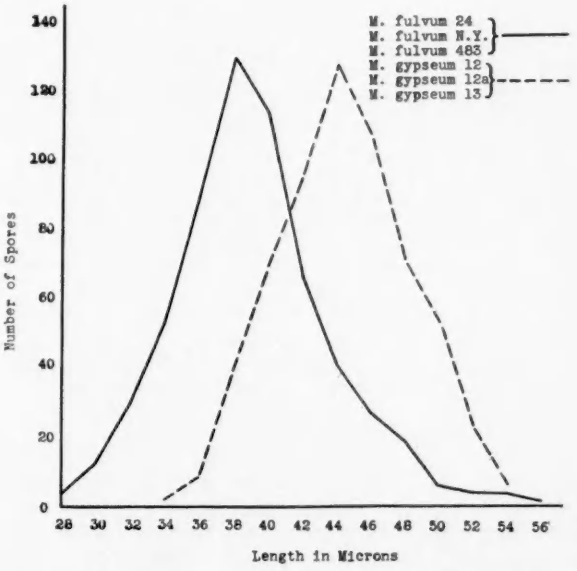


Fig. 4.—Comparison of the lengths of 600 macroconidia: 200 each from M. fulvum 24, N. Y. and 483; 200 each from M. gypseum 12, 12a and 13.

although its range lies within that of the other curves. Because of the similarity of the curves in these isolations, I considered M. lanosum and M. felineum as one species. The marked similarity of these two fungi has been noted before. While most authors have kept the two specific names lanosum and felineum, Langeron and Milochevitch [5] reduced the two to synonomy and retained as the valid name M. felineum, as they considered it the first named species.

A comparison of the curves of groups III and IV is presented in figure 6. The spores of these species (M. obesum, M. simiae, M. equinum, M. pseudolanosum and M. aurantiacum) took an intermediate position between the limits of

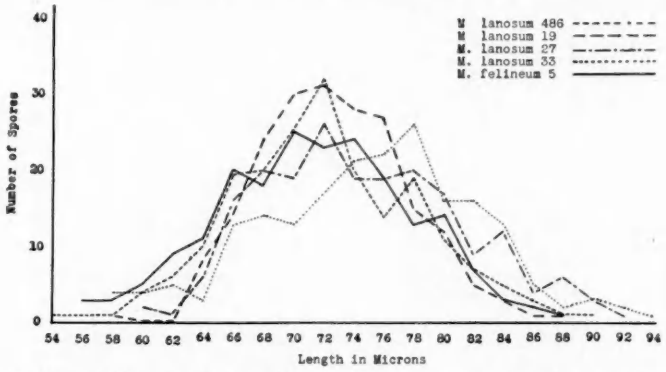


Fig. 5. Comparison of the lengths of 200 macroconidia each from four isolations of M. lanosum and one isolation of M. felineum.

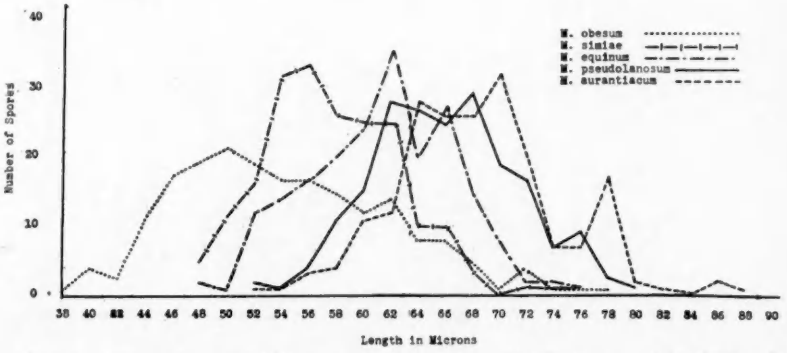


Fig. 6.—Comparison of 200 macroconidia each of M. obesum, M. simiae, M. equinum, M. pseudolanosum and M. aurantiacum.

28 and 94 microns of the spores of M. fulvum and M. lanosum, respectively. In figure 6 it is seen that the majority of the spores of M. obesum fall within the limits of from 48 to 56 microns; M. simiae, from 54 to 58 microns; M. equinum, from 62 to 66 microns; M. pseudolanosum, from 64 to 68 microns, and M. aurantiacum, from 64 to 72 microns. In this figure at least four curves (those for M. obesum, M. simiae, M. equinum and M. aurantiacum) are sharply defined and distinct, showing that the size of the macroconidia may be used for purposes of specific differentiation. The curve for M. pseudolanosum, however, is in close agreement with those for M. equinum and M. aurantiacum. However, although

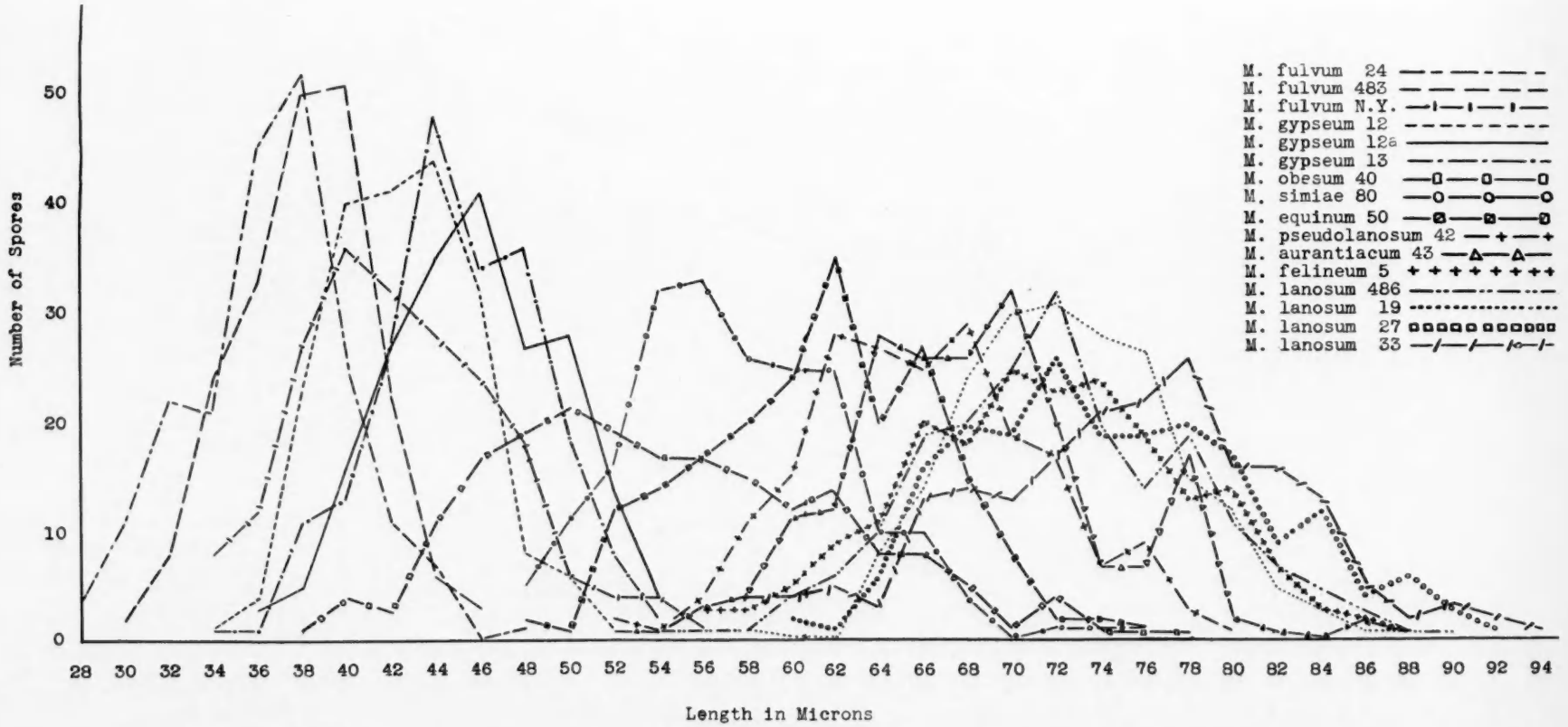


Fig. 7.—Comparison of the lengths of 200 macroconidia each from different isolations of eight species of Microsporum.

the macroconidia may be similar in size, other characters immediately separate these three species. M. pseudolanosum was easily distinguished from M. aurantiacum because of the rusty to orange spores of M. aurantiacum, while in M. pseudolanosum the spores were light buff. M. equinum also was distinguished easily from M. pseudolanosum. In M. equinum the macroconidia were borne from their supporting structures (conidiophores) in clusters, while in the latter a looser type of spore bearing was evident. A more detailed description of the several species mentioned in this paper, a description including not only the sizes of the spores but other distinguishing morphologic characters, will appear in a later paper.

For a better understanding of the relation of the curves considered in these various figures, a graph of all the curves is presented in figure 7. Here it will be seen that certain groupings are clearcut. For example, two species are indicated at the extreme left of the graph: one species to include M. fulvum, with spores of an average size of from 38 to 40 microns, the other to include M. gypseum, with spores of an average size of from 44 to 48 microns. Other curves in figure 7 show a third species, M. obesum, with spores from 48 to 56 microns long; a fourth species, M. simiae, with spores from 54 to 58 microns long; a fifth species, M. equinum, with spores from 62 to 66 microns long; and a sixth species, M. lanosum, with spores from 70 to 76 microns long. These curves are distinct, while the somewhat overlapping curves for M. pseudolanosum and M. aurantiacum, with spores averaging from 64 to 68 microns and from 64 to 72 microns in length, respectively, are not so convincing as to species rank. However, the additional characters which have been mentioned, i. e., the color of the macroconidia and the methods by which they are borne, are fully adequate for purposes of specific differentiation.

## SUMMARY

Studies to make possible the identification of species in the genus Microsporum involved a cultural, biometric and taxonomic consideration of a number of cultures. First, it was necessary to secure a consistent growth of the species on an artificial medium. Such a medium proved to be polished rice, on which a luxuriant growth was maintained which produced morphologic characters serving to distinguish the species. One such distinguishing character produced on rice was the large pluriseptate, fusiform, thick-walled spore, the macroconidium or fuseau. This spore was produced constantly and in great numbers. A more detailed discussion of the cultural study of this group of fungi has been given in a previous paper.[9]

Since the macroconidia proved to be the most prominent character of the genus, it was studied with the hope that it might be used in distinguishing species. Thus, the second consideration in this study of the genus Microsporum involved a biometric study of the Macroconidia, because of their variability in size. For this purpose the sizes of the spores were plotted for the various cultures studied. By comparing these curves six species were apparent: M. fulvum, M. gypseum, M. obesum, M. simiae, M. equinum and M. lanosum. The curves for M. pseudolanosum and M. aurantiacum were not as convincing as to

species rank. Fortunately, however, additional morphologic characters are available which, when taken as a whole, tend to strengthen the concept of a given species. Such characters as color of the spore, general shape, thickness of the wall, type of the wall (whether smooth or echinulate), the manner in which the spores are borne on their supporting structures (conidiophores) and the type of conidiophore all are necessary for a complete and easy segregation of species in any group of the fungi imperfecti.

Thus a third consideration in the study of the genus Microsporum would involve the gathering of all morphologic data and their presentation in a truly taxonomic treatment of the genus. With the foundation of a cultural and biometric study of several cultures, I have prepared such a taxonomic treatment for Microsporum, in which all the available morphologic characters will be considered and a key to the species will be presented, with the hope that it may prove of value to other investigators. This final paper will appear later.

This work was carried on under the direction of Prof. W. H. Weston Jr.

# LXXIV. SENSITIZATION OF ANIMALS TO PLANT OILS

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ST. LOUIS

Bloch and Steiner-Wourlisch [1] were the first to sensitize guinea-pigs to primrose by contact. Since then Mayer [2] has sensitized them in the same manner to para-phenylene-di-amine, Jadassohn,[3] to phenylhydrazine, and Simon and his associates,[4] to poison ivy oil. That sensitization can be produced in certain human beings by repeated contact with a substance has been shown by Strauss,[5] who sensitized infants to poison ivy; by Müller,[6] who used ursol (para-phenylene-di-amine), and by Silverberg,[7] who used mesotan (the methyloxymethyl ester of salicylic acid). Although the mechanism for producing hypersensitivity in man may not be the same, the condition occurs in a manner parallel to that noted in animals.

After a study of guinea-pigs sensitive to ivy, Simon and his associates [4] pointed out that the entire skin of the animal seemed to be sensitized. This was also noted by Bloch and Steiner-Wourlisch [1] with guinea-pigs sensitive to primrose and it is usually true in human beings. It is known, however, that there is some localization of contact sensitization in human beings, as can be shown at times with patch tests on various areas over the body. It is also not unusual to find contact dermatitis exclusively on one part of the body, such as the face, although

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Studies, observations and reports from the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, Department of Dermatology, service of Drs. M. F. Engman and W. H. Mook.

The oils used in this work were prepared in collaboration with Morris Moore, Ph.D., mycologist to the Barnard Free Skin and Cancer Hospital.

1. Bloch, B., and Steiner-Wourlisch, A.: Die Sensibilisierung des Meerschweinchens gegen Primeln, Arch. f. Dermat. u. Syph. **162**:349, 1930.

2. Mayer, R. L.: Die Ursolidiosyncrasie des Meerschweinchens, Arch. f. Dermat. u. Syph. **163**:223, 1931.

3. Jadassohn, W.: Sensibilisierung der Haut des Meerschweinchens auf Phenylhydrazin, Klin. Wchnschr. **9**:551, 1930.

4. Simon, F. A.; Simon, M. G.; Rackemann, F. M., and Dienes, L.: The Sensitization of Guinea Pigs to Poison Ivy, J. Immunol. **27**:113, 1934.

5. Strauss, H. W.: Artificial Sensitization of Infants to Poison Ivy, J. Allergy **2**:137, 1931.

6. Müller, A.: Sensibilisierungsversuche mit Ursol, Dermat. Ztschr. **61**:241, 1931.

7. Silverberg, M. G.: The Sensitization of the Skin to Mesotan, Arch. Dermat. & Syph. **21**:166 (Feb.) 1930.

several other areas, such as the hands and arms, have been exposed at the same time. However, this is usually not true when poison ivy is the contact substance.

## MATERIALS AND TECHNIC

The oils used in these experiments were acetone extracts prepared as described by Brown, Milford and Coca [8] and by Engman, Moore and Kile.[9] All solutions were made by volume in acetone.

Four guinea-pigs were painted with a 50 per cent solution of poison ivy oil after the hair had been pulled out by hand twenty-four hours previously. A stripe of oil was made across the intact skin of the abdomen with a camel's hair brush. This was repeated daily for six days. Four rabbits were treated in the same manner. Nine other guinea-pigs were treated similarly each day for three days. Four animals were painted for six days with 50 per cent dwarf ragweed oil, and six others were painted on nine successive days. Eight were painted for six days with 50 per cent orris root oil, four for six days with 50 per cent giant ragweed oil and four for six days with 50 per cent sage oil. Four guinea-pigs painted with acetone on six successive days showed no change.

Two weeks after the last application all the animals were tested by painting a stripe across the abdomen with a 5 per cent solution of the oil, as were also the control animals. Two controls were used for each group tested.

It was found that all the pigs painted six times with ivy oil exhibited a typical area of dermatitis within twenty-four hours. This persisted for forty-eight hours and slowly faded during the following week, the skin finally desquamating. The dermatitis consisted of a stripe of erythema, with tiny vesicles, at the test site. The test site need not be the site at which the previous paintings were done. Of the animals painted three times, two showed no more reaction than the controls, and two died during the experiment. At autopsy the essential change noted was acute nephritis with edema and hemorrhage into the kidney. The other organs were apparently normal. The five remaining guinea-pigs showed exactly the same reactions as those that had been painted six times. Biopsies made of the affected areas twenty-four hours after painting showed typical dermatitis, consisting of edema of the upper portion of the cutis, vascular dilatation and intracellular and extracellular edema of the epidermis, with beginning vesicle formation. The animals showed the same reaction when tested four months later. The ivy controls showed a faint, transient erythema, which disappeared within forty-eight hours and in no way approached the dermatitis produced in the treated animals.

The four animals painted six times were tested with the saponifiable and unsaponifiable fractions of the ivy oil, as well as with the whole oil. These were prepared as has been previously described [9] and were merely the two fractions resulting from saponification with sodium. It was found that the unsaponifiable fraction produced a dermatitis similar to that produced by the whole oil, though not quite so marked. The saponifiable fraction produced no reaction.

When the four rabbits were tested with both a 5 per cent and a 25 per cent solution of ivy oil, no reaction was noted other than the transient erythema also seen on the control animals. None of the guinea-pigs painted with orris root oil, sage oil or giant ragweed oil, or the controls, showed any reaction on

8. Brown, A.; Milford, E. L., and Coca, A. F.: Studies in Contact Dermatitis, J. Allergy **2**:301, 1931.

9. Engman, M. F., Jr.; Moore, M., and Kile, R. L.: Contact Dermatitis, South. M. J. **28**:442, 1935.

being tested with 5 per cent, 12.5 per cent and 25 per cent dilutions. Eight of the ten guinea-pigs treated with dwarf ragweed oil showed no reactions to the same dilutions. However, two of the animals showed an area of dermatitis when tested with 5 per cent and 25 per cent dilutions. This persisted for several days and was definite, though not so marked as that seen in the guinea-pigs sensitized to ivy. Of the two, one had been previously painted six and the other nine times. The controls showed no reaction.

## COMMENT

The observation that guinea-pigs could be made sensitive to poison ivy confirms the work of Simon and his associates.[4] It was demonstrated, further, that previous contact as well as a lapse of time is necessary for the production of contact sensitivity. It is apparently much easier to produce sensitivity with poison ivy oil than with other plant oils. The reaction takes place at least from four to six months after the contact is begun and probably much later. This has been shown by Bloch and Steiner-Wourlisch,[1] and Simon and his associates,[4] as well as in this study. It was found that rabbits are not sensitized to poison ivy, nor guinea-pigs to orris root, giant ragweed or sage oils. This has been noted by others.[10] It is difficult to explain why only two of the guinea-pigs tested with dwarf ragweed reacted. Perhaps the technic should have been varied somewhat, or there may be some inherent variation in the animals. It is, at any rate, comparatively easy to sensitize guinea-pigs to poison ivy. Sensitization occurs more regularly with concentrated oil and is more certain to occur the longer the series of original applications. Hence, two of the nine animals painted only three times did not react on subsequent testing. Evidence is also presented that the unsaponifiable fraction of ivy oil contains the active principle of the oil.

## CONCLUSIONS

Guinea-pigs were sensitized to poison ivy oil by application to the intact skin.

Rabbits were not similarly sensitized.

Guinea-pigs did not become sensitive to orris root, giant ragweed or sage when treated in this manner.

Two of nine guinea-pigs had definite reactions after previous application of dwarf ragweed oil.

NOTE.—Since this paper was submitted for publication two important articles on the subject have appeared, one by Brunsting and Bailey[11] and the other by Kobayashi.[12]

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10. Simon, F.: Personal communication to the author.

11. Brunsting, L. A., and Bailey, R. J.: Ragweed (Contact) Dermatitis Produced Experimentally in the Guinea Pig, J. Allergy **6**:547 (Sept.) 1935.

12. Kobayashi, Y.: Sensitization of Guinea-Pigs to Rhus Vernicifera and to Japanese and Chinese Lacquers, Jap. J. Dermat. & Urol. (Abstr. Sect.) **37**:92 (April) 1935.

# ARTERIAL EMBOLISM FOLLOWING INTRAMUSCULAR INJECTION OF A BISMUTH PREPARATION

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NEW YORK

Bismuth preparations have been used extensively by intramuscular injection for spirocheticidal purposes since 1922. The first instances of arterial embolism were reported before the Schlesische Dermatologische Gesellschaft by Freudenthal [1] in 1923. The literature now contains accounts of some fifty cases, reported mainly from France and Germany. In the United States, Gammel [2] has noted five, and De Wolf [3] two, such accidents. Similar pictures have been observed following the intramuscular injection of mercury, but the pathogenesis had not been understood.[1]

## REPORT OF A CASE

P. C., a white man aged 38, had begun antisyphilitic treatment seven years previously because of increasing deafness, perforation of the nasal septum and a positive Wassermann reaction of the blood. Since then he had received numerous but irregular courses of treatment with neoarsphenamine and bismuth, the Wassermann reaction of his blood becoming frequently but not consistently negative.

The fifth injection of the present series was given on March 3, 1935, at the inner angle of the upper outer quadrant of the right buttock through a 20 gage 1½ inch (3.75 cm.) needle. It consisted of 1 grain of bismuth subsalicylate suspended in 1 cc. of peanut oil. Aspiration was not attempted. The patient immediately felt severe lancinating pain, which radiated throughout the buttock and down the thigh, but he made no complaint. He was able to walk 1½ miles (2,414 meters) to his home, but then he went to bed because of pain and inability to move the affected limb. The buttock was red, hot, greatly swollen and very tender. The patient felt feverish and was unable to sleep because of his discomfort.

When he was seen on the next day at his home, about seventeen hours after the injection, he appeared to be fairly comfortable. The temperature, pulse, and respiration were normal. The pain was only occasional and not so severe as it was at first. The swelling had gone down, and the redness had disappeared.

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From the department of syphilology, service of Dr. Joseph Lebenstein, the Hospital for Joint Diseases.

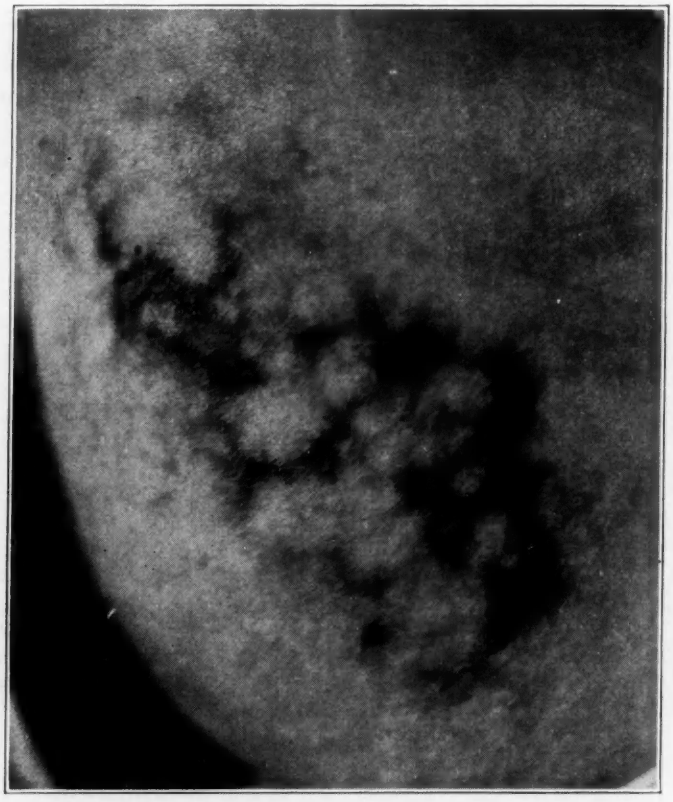
1. Freudenthal, W.: Lokales embolisches Bismogenol-Exanthem, Arch. f. Dermat. u. Syph. **147**:155 (April) 1924.

2. Gammel, J. A.: (*a*) Arterial Embolism: An Unusual Complication Following the Intramuscular Administration of Bismuth, J. A. M. A. **88**:998 (March 26) 1927; (*b*) Local Accidents Following the Intramuscular Administration of Salts of the Heavy Metals, Arch. Dermat. & Syph. **18**:210 (Aug.) 1928.

3. De Wolf, H. F.: Arterial Embolism Complicating Intramuscular Injection of Mercurial and Bismuth Salts, Urol. & Cutan. Rev. **37**:423 (June) 1933.

Covering the buttock was an arborescent violaceous network roughly elliptic and about 8 by 4 inches (20 by 10 cm.), which had appeared about eight hours after the onset of the reaction. The skin was hot and exquisitely tender. No nodules could be felt. The limb could be moved spontaneously, but motion was slow and guarded. There were no changes in sensation or reflexes. Two days later he was able to get about.

When he was observed at the clinic ten days after the injection, the patient walked normally. The striae of the lesion had become more livid and were ele-



Appearance of the lesion ten days after the injection of bismuth subsalicylate.

vated, cordlike and somewhat warm and tender. Here and there on the network were about eight grayish-black areas, each about ¾ inch (1.9 cm.) in length. Some of these necrotic spots, according to the patient, had recently discharged yellowish fluid and blood and then dried up. The skin about the mesh was normal in appearance and to palpation except for some new punctate spots (fig.).

Twenty days after the injection the network had lost its cordlike feel, was considerably faded and was no longer warm or tender.

Thirty days after the injection the buttock showed only a delicate tracery of fine violet lines. Bismuth subsalicylate was administered intramuscularly near the site of the former injection without any ill effects.

COMMENT

This course is fairly typical of that in the cases of less severe involvement. The marble-like appearance of the lesion is characteristic and has been likened to livedo racemosa or to cutis marmorata, a rare disease of the skin caused by hyperemia of the cutaneous capillaries. In the cases of more severe involvement the condition progresses until gangrene of the skin or of the muscles occurs, so that a large part of the buttock may be involved. A blackish eschar separates, leaving a surface which granulates sluggishly and heals slowly because of the impaired vascularity. In some cases there have been muscular paralyses and sensory changes, probably due to involvement of the nerves through the comitant artery of the sciatic nerve.[2] In these the recovery of function is slow, may not occur at all and may be followed by trophic ulcers of the foot.[2b] Embolism through anastamoses of the gluteal and internal pudendal arteries may cause superficial gangrene of the rectum, bladder, vagina,[2b] vulva, penis, scrotum and thighs.[4]

Early biopsy shows acute inflammatory changes and edema about the affected arteries, which are plugged by emboli of crystals of the bismuth salt used. If a soluble preparation has been employed, the endarteritis induced by caustic action causes thrombosis. Behind the plug the vessels are dilated by a homogeneous mass in which the cellular elements of the blood have decomposed, releasing hemoglobin. Escape of this pigment into the perivascular tissues causes the characteristic violaceous hue. Later, ischemic changes follow this deprivation of blood supply.[5]

Roentgenography,[6] with proper calibration and exposure, shows a closely meshed plexus, thus proving that not only the visible livid vessels of the skin but also the subdermal vessels are filled with an opaque medium.

Treatment is symptomatic. If there is deep gangrene, surgical intervention [7] may be resorted to in order to hasten the separation of the slough.

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4. Payenneville and Castagnol: Quatre nouveaux cas de dermite livédoïde et gangréneuse de Nicolau à la suite d'injection de Quinby, Bull. Soc. franç. de dermat. et syph. **37**:1027 (July) 1930.

5. Freudenthal.[1] Gammel.[2b]

6. Moncorps, C.: Beitrag zur Kenntnis der Embolia cutis medicamentosa nach intramuskulären Bismogenolinjektionen, Dermat. Wchnschr. **95**:976 (July 2) 1932. Merenlender, J.: Zur Kenntnis der Embolia cutis arterialis medicamentosa (bismutica), Arch. f. Dermat. u. Syph. **167**:708 (March) 1933.

7. Gougerot, H., and Quénu, J.: Traitement chirurgical de la gangrène massive par injection artérielle du bismuth, Ann. d. mal. vén. **21**:741 (Oct. 9) 1926. Martins de Castro, N.: Embolie artérielle bismuthique avec lésions graves de la peau l'étude clinique et anatomo-pathologique, Ann. de dermat. et syph. **10**:161 (Feb.) 1929.

This is a rare accident but not an easy one to avoid. In many of the reported cases aspiration was performed, and though no blood was seen this complication followed. Blood rises slowly through a narrow gage needle and an oily vehicle. Gammel [2b] offered the best prophylaxis: Aspiration is performed first into a syringe containing saline solution. If no bleeding is noted the syringe is detached and another syringe containing the bismuth preparation is attached to the needle.

# PATHOGENESIS OF THE CUTANEOUS COMPLICATIONS OF VARICOSE VEINS

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The pathogenesis of the cutaneous complications of varicose veins is usually explained on the basis of chronic passive congestion of the skin and of the subcutaneous tissues, which results from venous stasis in the varicose superficial vessels. Many of the clinical features of these complications, however, are not compatible with this explanation and support, rather, the interpretation, expressed in previous publications,[1] that the cutaneous lesions are of inflammatory origin, arising by extension from phlebitis of the varicose veins. One of the principal arguments in favor of this hypothesis is the topographic relationship between the cutaneous lesions and the varicose trunks.

Attention has been called to the value of infra-red photography[2] for visualizing subcutaneous varicosities. By means of this method it is possible to demonstrate an immediate topographic association of varicose eczema and ulcer with subjacent dilated trunks. In the accompanying illustrations are seen various types of cutaneous lesions associated with varicose veins. The infra-red photographs of the same limbs show the distribution of the varices. In each of the pairs of photographs it may be seen that immediately beneath the cutaneous lesion there is a dilated venous trunk or pool. This topographic proximity of cutaneous lesions and varicose trunks speaks convincingly against stasis as the cause of the cutaneous condition. If stasis resulted from such a varicosity, it would be in the tissues about the capillary bed which drains into the varicose vein and not in the skin overlying

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From the Peripheral Circulatory Clinic, Department of Surgery, Northwestern University Medical School.

1. Zimmerman, L. M.: Complications and Treatment of Varicose Veins, Illinois M. J. **59**:60 (Jan.) 1931; Phlebitis, Thrombosis, and Thrombophlebitis of the Lower Extremities, Surg., Gynec. & Obst. **61**:443 (Oct.) 1935.

2. Zimmerman, L. M., and Rattner, H.: Infra-Red Photography of Subcutaneous Veins, Am. J. Surg. **27**:502 (March) 1935.

the trunk itself. Direct pressure of the varix on the adjacent skin might be mentioned as a factor, but comparable cutaneous lesions do not occur elsewhere over soft tumors or other pressure points.

The topographic relation between the vein and the cutaneous lesion confirms the belief that the complications of varicose veins are of inflammatory origin and that a direct sequence of events can be traced from the varicose vein to the final lesion. The first step in the chain

Fig. 1 (A. H., a woman aged 38).—The patient had a "phlebitic ulcer" five years before the photographs were taken. The conventional photograph shows a pigmented, indurated scar above the internal malleolus and an indurated "plaque" in the middle third of the leg. The infra-red photograph shows a network of varicose veins immediately beneath both the scar and the induration.

is phlebitis, which constitutes the most common complication of varicose veins. The frequency of phlebitis is explained by the stasis and anoxemia within the vessel and the changes in the intima, all of which

predispose to the localization of blood-borne organisms. These organisms reach the vessels from focal or intercurrent infections, and may remain inactive between successive attacks of inflammation. As a result of recurring localized phlebitis, the inflammation extends to the adjacent skin and subcutaneous tissues and a patch of subacute cellulitis appears.

Fig. 2 (H. K., a woman aged 40).—Old phlebitis of the deep veins was followed by inflammation of the superficial veins. The conventional photograph shows pigmented areas on both legs and extensive scarring on the inner aspect of the left ankle. The infra-red photograph shows the coincidence of distribution of varices and cutaneous involvement.

With repeated recurrence and subsidence of these attacks of cellulitis, permanent irreversible changes take place, including pigmentation, infiltration, cicatrization, atrophy and adherence of the integument to the

deeper structures. Superimposed on these changes are the eczemas, induration, dermatoses and ulcers, representing the end-stages of this inflammatory sequence.

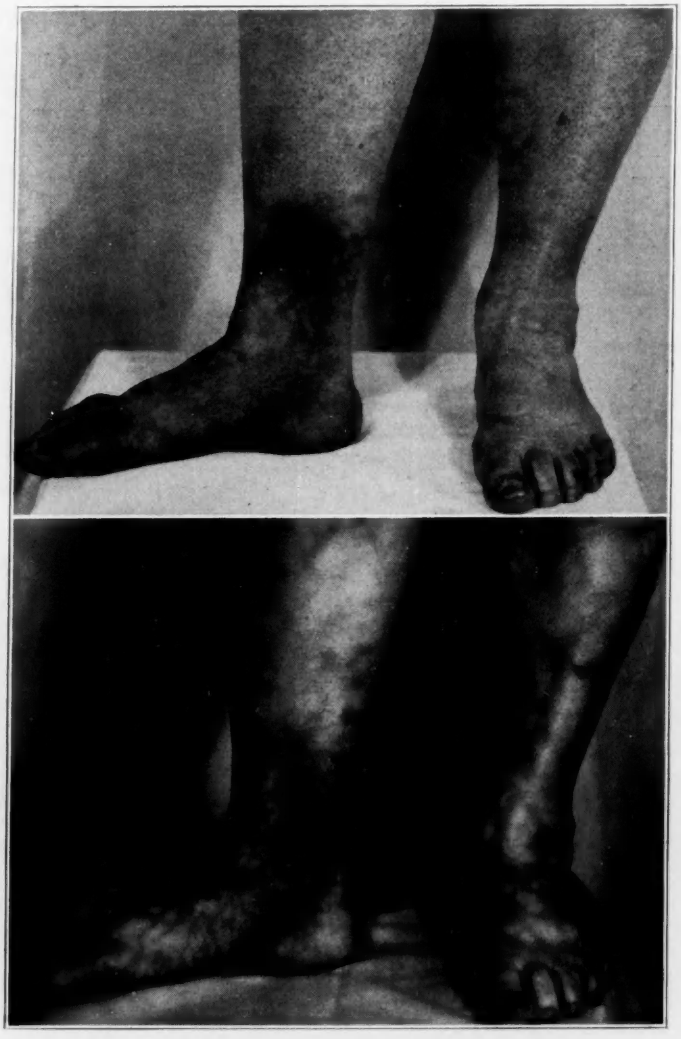

Fig. 3 (N. J., a woman aged 42).—The patient had old puerperal phlebitis and a healed varicose ulcer. The infra-red photograph shows large varicose pools immediately in the center of the indurated zone, beneath the scar of the ulcer.

Fig. 4 (F. P., a woman aged 45).—The patient had eczema, induration and discoloration of both legs. The photographs show the topographic coincidence of veins and cutaneous lesions and the absence of varicosities below the pigmented areas.

Fig. 5 (C. L., a woman aged 74).—The patient had eczema, with beginning ulceration and large varices immediately subjacent to the lesion, which is not in the most dependent portion of the leg.

SUMMARY

Infra-red photographs of varicose veins and their cutaneous complications reveal an immediate topographic relationship between the dilated trunks and the overlying cutaneous lesions. This is offered as further proof of the contention that these cutaneous lesions are not the result of chronic passive congestion, as is usually stated, but are of inflammatory origin, arising by direct extension from infections within the varicosities.

Fig. 6 (W. C., a woman aged 45).—A large deep callous ulcer is seen near the middle of the left leg, and there is induration of both legs. Note the absence of varices on the anterior aspect of the left leg, corresponding to the area of relatively intact skin.

Miss Madge Walsh, of the department of photography of the Northwestern University Medical School, assisted in preparing the photographs.

# FIXED ARSENICAL ERUPTION

## SENSITIVITY TO TRYPARSAMIDE AT SITES OF PIGMENTATION FOLLOWING DERMATITIS DUE TO SILVER ARSPHENAMINE

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The occurrence of a fixed eruption due to tryparsamide is a rare complication of antisyphilitic treatment, the case reported by Robinson [1] being the only one on record. For some time I have had under observation a patient in whom sensitivity to tryparsamide developed at the sites of pigmentation which remained after arsphenamine dermatitis sustained four years previously. It was found that the patient was sensitive to all trivalent arsenicals over the entire cutaneous surface, as evidenced by patch and intradermal tests, and to tryparsamide only in the pigmented areas.

### REPORT OF CASE

W. Y., a white man aged 40 years, was first seen in June 1933, when he requested continuation of antisyphilitic treatment. He stated that he had a penile lesion in 1919, which healed in five or six weeks. No secondary lesions were noted and no treatment was given. In 1925 he became depressed and nervous. The Wassermann reaction of his blood was positive, and treatment with neoarsphenamine was started. Symptomatic response was good, and no reaction to treatment was noted until 1929. Between 1925 and 1931 the patient received approximately thirty injections of neoarsphenamine, twenty of silver arsphenamine, fifty of a bismuth preparation and fifty of an insoluble preparation of mercury.

In 1929 he noted some itching and a patchy dermatitis of the hands, face and upper part of the trunk after each injection of arsphenamine. After an injection of 0.2 Gm. of silver arsphenamine he had fairly severe generalized dermatitis with exfoliation, which lasted for from three to four weeks. There remained pigmented macules of varying sizes over the arms, upper part of the trunk, face and neck, many of them at the sites of the patchy dermatitis. From 1929 to 1932 alternate courses of tryparsamide and heavy metal were given. When I first saw the patient he had received approximately thirty-five injections of tryparsamide. After the last six or eight he had noted some edema and livid erythema, with moderate itching, at the sites of the pigmented macules.

The Wassermann reaction of the blood had been negative since 1927. The patient had never permitted an examination of the spinal fluid to be made. It is certain that no tryparsamide was administered before the attack of arsphenamine dermatitis.

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From the Department of Dermatology and Syphilology, University of Pennsylvania School of Medicine Dr. John H. Stokes, Director.

1. Robinson, H. M.: Fixed Dermatitis Due to Tryparsamide, Am. J. Syph. & Neurol. **17**:507 (Oct.) 1933.

*Physical Examination.*—The patient was a flabby, asthenic person looking considerably older than the stated age. Bluish-brown macules varying in size from 1 to 4 cm. were scattered over the skin of the arms, trunk, neck and face. The macules were round or ovoid and sharply marginated. The mucous membranes showed no pigmentation. Except in regard to the central nervous system, the rest of the examination gave negative results. The positive neurologic findings included sluggish and incomplete reaction of the pupils to light, hyperactive, bilaterally equal tendon reflexes, moderate slurring of the test phrases and some loss of memory. The reaction to questioning and examination was alert. The patient showed marked introspective tendencies and a surprising knowledge of methods of antisyphilitic treatment. The Wassermann and Kahn reactions of the blood were repeatedly negative. Examination of the spinal fluid in August 1934 gave negative results with all four standard tests.

*Further Course.*—Tryparsamide therapy was continued, with observation of the skin a day or two after each injection. A syringe free from arsphenamine was used. Within from twelve to fifteen hours after each injection there developed at the site of the fixed eruption an urticarial reaction and a purplish erythema exactly simulating that seen in phenolphthalein eruption. Ingestion of phenolphthalein produced no effect on the skin. With succeeding injections of tryparsamide the local reaction became more pronounced and the patient complained of mild general malaise and drowsiness. After having received thirteen injections he refused further intravenous therapy. A distinct variation in the reactions of the skin to 1 Gm. and to 3 Gm. of tryparsamide was noted, the reactions to the larger amount being much more marked.

*Results of Patch and Intradermal Tests with Tryparsamide, Neoarsphenamine, Silver Arsphenamine, Bismarsen and Sodium Bismuth Tartrate.*—All the arsphenamines used produced a definitely positive reaction to patch tests (sharp erythema and vesicles) within twenty-four hours on the normal skin and at the sites of pigmentation. The reaction in both areas was sharply localized to the portion of skin in contact with the gauze soaked in the testing material (30 per cent solution). In the intradermal tests on pigmented areas there was a tendency for the entire area to react, but the reaction about the site of the injection was much more marked. Patch and intradermal tests with a 30 per cent solution of tryparsamide produced no reaction on the normal skin; at the sites of pigmentation there occurred a reaction exactly like that seen after an intravenous injection of tryparsamide, edema and purplish erythema appearing evenly in the entire macule, with no extension to the surrounding normal skin. Examination with a lens revealed no vesicles, and the immediate site of contact with gauze soaked with tryparsamide could not be made out. The reaction developed more slowly than with the arsphenamines and did not begin to subside until forty-eight hours after the removal of the patch. There was no reaction to patch or intradermal tests with a 10 per cent concentration of soluble sodium bismuth tartrate.

*Biopsy.*—A portion of one of the pigmented patches was removed four weeks after the administration of 3 Gm. of tryparsamide intravenously, no gross evidence of the reaction being present. Fixation and staining were by the routine formaldehyde and hematoxylin-eosin method. The epiderm was somewhat thin and there was considerable pigment in the basal layers. There was no spongiosis or intradermal formation of vesicles. The outstanding changes were in the papillae and upper portion of the corium, which showed marked edema, a sparse round cell infiltrate and numerous chromatophores. The appendages were normal.

*Biospectrometric Analysis* (Dr. L. Edward Gaul, New York).—Analysis was made of a portion of the skin fixed with formaldehyde. The metallic elements in the specimen were present in normal quantities with the exception of lead and manganese, the density of the lead line indicating 1 plus retention and that of the manganese line a slight excess. The significance of the slight excess of manganese was not apparent, and the possibility of contamination from the formaldehyde was considered. It is to be noted especially that there was no retention of silver or arsenic, indicating that no local fixation of tryparsamide had taken place.

## COMMENT

The significant findings in the case may be outlined as follows: (1) a fixed macular pigmentation persisting after an exfoliative dermatitis due to silver arsphenamine; (2) a livid, erythematous urticarial reaction which developed gradually and became increasingly severe after successive injections of tryparsamide; (3) eventual complaint of general malaise and drowsiness; (4) universal sensitivity of the entire skin to arsphenamines, as evidenced by positive reactions to patch and intradermal tests, and (5) sensitivity to tryparsamide localized at the sites of the fixed eruption.

In the case of fixed eruption due to tryparsamide reported by Robinson,[1] patch tests with tryparsamide on both the involved and the uninvolved skin gave negative results. This is not surprising, as fixed eruptions due to drugs are markedly capricious in this regard.[2] An analogous case has been reported by Gougerot and Boudin,[3] in which erythroderma of the hands and feet was produced by injections of acetylarsan, a pentavalent arsenical, nine years after generalized erythroderma due to neoarsphenamine, a trivalent arsenical. In this case apparent universal sensitivity to acetylarsen was present, as evidenced by patch tests. The eruption was not fixed, in the usual sense.

I believe that the distinctly different types of reaction to arsphenamine and tryparsamide seen in the patch tests in my case are worthy of an attempt at interpretation. The reaction to arsphenamine was of the eczematous type, superficial and sharply limited to the portion of the skin in direct contact with the allergen. It developed rapidly and started to subside as soon as the patch was removed. The reaction to tryparsamide developed more slowly (in forty-eight hours) and persisted unabated for two days after removal of the patch. It was not superficial and was distinctly not limited to the site of the contact with tryparsamide, and there was no vesicle formation. It seems entirely possible that the reaction developed as a consequence of absorption of the tryparsamide, since the site of shock tissue was principally in the

2. Sulzberger, M. B.; Wise, F., and Wolf, J.: A Tentative Classification of Allergic Dermatoses, J. A. M. A. **104**:1489 (April 27) 1935.

3. Gougerot, H., and Boudin, G.: Erythrodermie arsénicale localisée aux mains et aux pieds, Ann. d. mal. vén. **29**:240 (June) 1934.

upper portion of the cutis, the superficial portion of the epiderm remaining grossly unaffected by the passage of the drug through it. The classification of allergic dermatoses, recently advanced by Sulzberger, Wise, and Wolf,[2] is based on the site of the shock tissue, the reaction time, the characteristic lesion and pathologic process, and the type of diagnostic test most suitable. The reaction of my patient to arsphenamine belongs to type I of this classification, eczematous reactions in which the site of the shock tissue is the epiderm, though perhaps originally to type IV, miscellaneous reactions, including fixed drug eruptions. The reaction to tryparsamide was of type IV.

It seems not improbable that in the original sensitivity to arsphenamine both the epiderm, with its exfoliative dermatitis, and portions of the cutis, with their fixed eruption and pigmentation, were the sites of shock tissue, and that the gradually developing sensitivity to tryparsamide manifested itself in the portions of the cutis which were previously the shock sites for arsphenamine. One may speculate as to whether or not the patient would have had a fixed tryparsamide eruption had not the previous heterophile sensitization with arsphenamine occurred. The fact that no previously unaffected sites became the seat of the tryparsamide eruption is significant. This may indeed be another example of the Sanarelli phenomenon [4] as applied to the skin, in which previous sensitization to a heterophile substance leads to reaction at the affected site to a large variety of normally nontoxic substances.[5]

SUMMARY

A case is reported of a fixed eruption due to tryparsamide occurring only at the sites of pigmentation following an arsphenamine eruption sustained four years previously. The possible significance of this superimposed sensitivity, with the cutis as the site of shock tissue, is briefly discussed.

4. Sanarelli, G.: Le choléra expérimental, Ann. Inst. Pasteur **38**:11, 1924.

5. The Synergistic Etiology of Poliomyelitis, editorial, J. A. M. A. **103**:757 (Sept. 8) 1934.

# EXPERIMENTAL ARSPHENAMINE DERMATITIS

## REACTION TO ARSPHENAMINE IN NORMAL GUINEA-PIGS AND IN GUINEA-PIGS GIVEN STAPHYLOCOCCUS TOXIN

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In a previous communication [1] certain preliminary observations were made on the nature of arsphenamine [2] dermatitis as produced in guinea-pigs.

It was noted that sensitization to arsphenamine was easily produced in the guinea-pigs used in this experiment. Two brands of arsphenamine were used. It was further noted that different brands of neoarsphenamine and different lots of the same brand of arsphenamine varied greatly in their power to cause cutaneous sensitization of normal guinea-pigs fed a diet high in vitamin C. Furthermore, the degree of sensitivity developed seemed higher when a single lot of arsphenamine of a high sensitizing index was used throughout the sensitizing period. A considerable variation in reactivity was encountered when a subsequent injection of arsphenamine was given intravenously. When the second "sensitizing" intradermal injection was made with two different brands of arsphenamine and the subsequent intravenous injection was made with that brand of arsphenamine which had been used both for the preliminary and for one of the second sensitizing injections, the focal reactions were distinctly more frequent and more severe in the area in which the same brand of arsphenamine had been given intradermally. When a different brand of neoarsphenamine was used for the intravenous testing, the reactions were less frequent and less marked. This, of course, suggested that sensitization may be confined more or less to the individual brand of arsphenamine causing the sensitization. It also suggested that intravenous testing in human beings, in whom the second sensitizing injection is apparently not necessary to produce dermatitis,

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From the section on Dermatology, Department of Medicine, Royal Victoria Hospital.

1. Cormia, F. E.: Experimental Arsphenamine Dermatitis: I. Canad. M. A. J. **34**:272 (March) 1936.

2. The terms arsphenamine and neoarsphenamine are used interchangeably throughout this report; neoarsphenamine, however, was the official drug used in each experiment.

may be superior to the intradermal test recently partially discredited. This confirms the similar statement made by Moore and his co-workers [3] on the clinical value of intravenous testing.

The localized nature of the reactivity in guinea-pigs to the intravenous injections of arsphenamine further indicated that a disturbance in local cellular equilibrium had been caused by the direct action of the arsphenamine solution. It was inferred that this was in part due to local injury to the tissue, since vascularly administered arsphenamine gave rise to a cutaneous flare only when the intravenous injection was preceded by two intradermal injections. In the present paper further observations are made on the nature of experimental arsphenamine dermatitis in guinea-pigs.

## REACTION TO ARSPHENAMINE IN NORMAL GUINEA-PIGS

EXPERIMENT 1.—Two groups of guinea-pigs were given injections of a single brand of arsphenamine, the two methods of injection of the previous experiment and that outlined by Sulzberger [4] being used. The arsphenamine was injected into an initial group of seven normal guinea-pigs and into a second group of six normal guinea-pigs procured from the same source one month after the first group. Of the first group of seven guinea-pigs, six were definitely sensitized, there being three 3 plus reactions, two 2 plus and one 1 plus. Of the second group of six guinea-pigs, but three reacted, there being two 2 plus reactions and one 1 plus reaction.[4a]

From experiment 1 the following conclusion was drawn: Different groups of guinea-pigs present considerable variations in the ability to become sensitized, these variations being independent of the diet and of the type of arsphenamine injected.

EXPERIMENT 2.—Six guinea-pigs were given injections of brand "A" of arsphenamine, twelve months old. Another six were given injections of brand "A" of arsphenamine, six months old. Five of the first six showed positive sensitization reactions. In the second group only three of the six animals reacted positively.

The conclusion was drawn that the age of the preparation may possibly be a factor in the ability to produce sensitization to arsphenamine in guinea-pigs.

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3. Moore, J. E.; Woo, S.; Robinson, H., and Gary, S.: Reactions of the Skin Following the Intradermal Injection of Arsphenamine: Postarsphenamine Dermatitis, Arch. Dermat. & Syph. **23**:74 (Jan.) 1931. Robinson, H.: Patch Tests in Determination of Arsphenamine Sensitization, South. M. J. **27**:845 (Oct.) 1934.

4. Sulzberger, M. B.: Hypersensitiveness to Arsphenamine in Guinea-Pigs: I. Experiments in Prevention and in Desensitization, Arch. Dermat. & Syph. **20**: 669 (Nov.) 1929.

4a. Reactions were tabulated as 1 plus when the area of erythema was 1 cm. in diameter, 2 plus when it was 2 cm. in diameter, 3 plus when it was the size of a quarter with or without a small central area of edema and 4 plus when it was the size of a silver dollar or larger, with a large area of central edema.

## REACTION TO ARSPHENAMINE IN GUINEA-PIGS GIVEN STAPHYLOCOCCUS TOXIN

The recent experimental work of Burky [5] suggested that certain products of infection effect changes in the organism which act as an adjunct in the production of sensitization.

Burky was able, by the simultaneous use of a highly powerful staphylococcus toxin, to sensitize rabbits to rabbit lens, a hitherto impossible procedure. The principles underlying this experiment are unknown; on the basis of innumerable clinical observations the products of infection are supposed to broaden the base of sensitivity. Burky had previously noted that immunity can be produced in rabbits by the intradermal injection of staphylococcus toxin. In the course of this experiment he accidentally observed that while an initial immunity to the toxin developed in the rabbits, continued injections caused increased reactions. This was subsequently found to be due to sensitivity to the broth in which the toxin was suspended and led to the later experiment with rabbit lens.

On the basis of this work it seemed expedient to determine, if possible, the effect of staphylococcus toxin in the production of cutaneous hypersensitivity to arsphenamine in guinea-pigs.

A preliminary group of control experiments were performed to determine the nature of the action of staphylococcus toxin. The Burnet toxin, prepared under the supervision of Dr. E. G. Murray, professor of bacteriology at McGill University, was used throughout. The toxin was kept at a constant level, about 7,000 Burnet units.

EXPERIMENT 1.—Four young adult guinea-pigs were given intradermal injections once weekly for six weeks of 0.1 cc. of the sterile filtered broth medium, in which the toxin was suspended for the first experiment. There were no cutaneous reactions to any of the injections.

Standardization of the action of the toxin in a series of twelve normal guinea-pigs was carried out as follows: various amounts of the toxin, from 0.1 cc. to 0.000005 cc., were injected intradermally into the abdomens of normal guinea-pigs once weekly for six weeks. A characteristic type of lesion was observed. A small dose, 0.001 cc. or less, resulted in the formation of a small inflammatory papule. When 0.001 cc. or more was given, a small necrotic central area also developed. Large doses (0.001 to 0.1 cc.) caused one of two types of lesion: (1) a hemorrhagic center with surrounding necrosis and a vivid red border of inflammation (with the largest doses there was an accompanying edema; later the large necrotic area became crust-covered and adherent to the underlying muscle tissue) or (2) a large central area of hemorrhagic necrosis with a faint grayish periphery and a surrounding pinkish inflammatory halo.

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5. Burky, E.: Studies on Cultures and Broth Filtrates of Staphylococci: I, II and III, J. Immunol. **24**:93, 115 and 127 (Feb.) 1933; Studies on Cultures and Broth Filtrates of Staphylococci: IV. Antitoxin Content of Rabbit Serums Immune to Staphylococcus Toxin and Precipitin Reactions to Such Serums, ibid. **25**:419 (Nov.) 1933; Production in Rabbit of Hypersensitive Reactions to Lens, Rabbit Muscle and Low Ragweed Extracts by Action of Staphylococcus Toxin, J. Allergy **5**:466 (July) 1934.

In seven of the twelve guinea-pigs the reactions of the skin to successive injections became more marked. This was noted particularly after the third and fourth injections. The later reactions were from one and one-half to two and one-half times as large as those of the initial injections. This occurred despite the fact that the same batch of toxin was used throughout, i. e., a toxin of diminishing strength. The strength of the toxin diminished so rapidly that after four weeks the size of the lesion produced by the initial injection in a series of three control animals was but half that of the lesion produced by the reaction to fresh toxin. Of the seven guinea-pigs which showed increased reactions to toxin of diminishing strength, four were included in the group of five which died of toxemia. All these seven guinea-pigs had injections of 0.005 cc. or over. The optimum concentration of toxin necessary to produce increasing reactions was from 0.01 to 0.05 cc.

For four of the seven animals with increasing reactions it was possible to give a subsequent control injection of 0.1 cc. of the filtrate from beef heart-peptone agar broth. In each instance a papule (from 4 to 12 mm. in diameter) appeared. In one instance a hemorrhagic center developed, and in another there was a small central area of necrosis. This experiment seems to indicate that the guinea-pigs had become slightly sensitive to the agar broth, since no reactions occurred when the broth was injected into animals of a control series.

The larger doses of toxin caused a general toxemia (chiefly vasculotoxic) and loss of weight. These guinea-pigs were also subject to pneumonia, three dying of toxemia, with multiple subcutaneous and visceral hemorrhages, two of toxemia and pneumonia and three of pneumonia.

Five cubic centimeters of blood was withdrawn from the heart of two of the guinea-pigs to determine the amount of antitoxin produced. In the first animal, which had received six injections of toxin, each of 0.001 cc., there developed 1,000 Burnet antihemolytic units of antitoxin. In the second guinea-pig, which was given similar injections but with a weekly dose of only 0.00005 cc., there developed less than 250 units of antitoxin (a negligible amount).

To determine the toxicity of the toxin two normal guinea-pigs were given intravenous injections of fresh toxin, the first of 0.01 cc. and the second of 0.001 cc. Both died within forty-five seconds.

In conclusion, the Burnet toxin is highly lethal for guinea-pigs. It causes characteristic reactions when injected intradermally, which are not reactions to the broth per se, but which may be increased reactions to the broth due to some unknown action of the toxin on the skin in particular and on the immunity mechanism of the body in general. When proper dosage is used, antitoxin in appreciable amounts can be demonstrated in the blood of guinea-pigs. A marked toxemia results when the injections are continued over a period of weeks. The toxin is vascularly toxic, causing a hemorrhagic necrosis in situ and distal hemorrhages in both the subcutaneous tissue and the viscera and rapidly causing death when given intravenously. The reaction is apparently similar to that occurring in rabbits,[6] since there was a marked pulmonary engorgement and resultant failure of the right side of the heart.

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6. Kellaway, C. H.; Burnet, F. M., and Williams, F. E.: The Pharmacological Action of the Exotoxin of Staphylococcus Aureus, J. Path. & Bact. **33**:889 (Oct.) 1930.

EXPERIMENT 2.—This experiment was made to determine the results of the simultaneous injection of the Burnet staphylococcus toxin and neoarsphenamine in guinea-pigs.

Five-hundredths cubic centimeter of a 7,000 unit[7] standard Burnet toxin was mixed with 0.1 cc. of a solution of neoarsphenamine prepared as in the previous experiments and containing 0.00015 Gm. of neoarsphenamine. This mixture was immediately injected intradermally into the depilated abdomen of a guinea-pig.

The method used by Burky was attempted but was not feasible. This consisted of adding to the freshly inoculated agar broth culture of staphylococci neoarsphenamine in sufficient quantity to make a 1:1,000 solution. Unfortunately, the aerobic conditions necessary for bacterial growth rapidly oxidized the neoarsphenamine. In addition, the concentration of the arsphenamine preparation required completely prevented the growth of the staphylococcus.

Eighteen normal guinea-pigs were selected for the experiment. In addition, sixteen from previous experiments were used to determine the effect, if any, of the toxin-arsphenamine mixture on preexisting sensitization.

*Group 1.*—This group consisted of three normal guinea-pigs and four others in which previous attempts to produce sensitization were unsuccessful, i. e., which could not be sensitized intradermally by the two injection method.

During the first week the toxin-arsphenamine mixture was given; then the toxin was injected alone once weekly for three injections, and then the neoarsphenamine was injected alone after one more week.

The reaction to the initial injection was an area of hemorrhage and edema the size of a quarter, with a small central area of necrosis. The following week similar-sized lesions were produced with the toxin alone, and the previously resistant guinea-pigs reacted also with a slight to moderate degree of erythema in the area in which sensitization with neoarsphenamine had been previously attempted. However, the next two weekly injections of toxin produced gradually diminishing reactions, and when the test dose of neoarsphenamine was given after another week no reactions were observed. The conclusion was drawn that the toxin did not have a definite sensitizing effect in previously unsensitizable guinea-pigs; in fact it seemed as if some other factor had intervened, since the three normal guinea-pigs could not be sensitized by the toxin-arsphenamine method.

*Group 2.*—This group consisted of five guinea-pigs which had shown weak sensitization reactions in previous attempts to produce sensitization. The method used was that used in group 1. The initial reactions were lesions the size of a quarter similar to those described for group 1. The following week the toxin alone was given, but in two guinea-pigs, in addition to the hemorrhagic and edematous local reaction to the toxin, markedly erythematous and edematous flares developed in the area of sensitization of the previous experiment. In a third guinea-pig in this series there developed a slight erythema. The subsequent history was one of diminishing reactions to the two last injections of toxin and a single 1 plus papular reaction to the last dose of neoarsphenamine.

The conclusion seemed justified that after the early flare-ups in the sites of previous sensitization there was an actual decrease rather than an increase in dermal sensitivity.

*Group 3.*—The group consisted of four guinea-pigs which had shown strongly positive sensitization reactions in the earlier experiments.

The method was that used for group 1.

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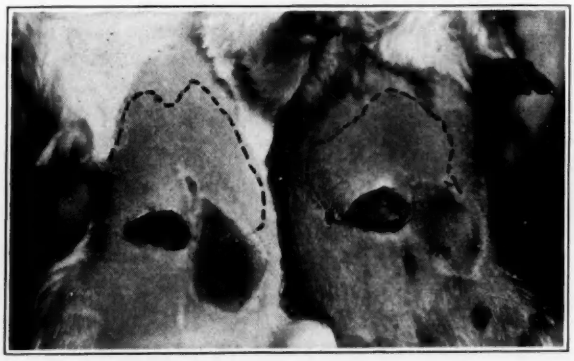
7. One cubic centimeter of a 1:7,000 dilution of toxin causes 50 per cent hemolysis in 0.1 cc. of a 10 per cent suspension of rabbit cells.

The local reactions to the toxin-arsphenamine mixture and to the toxin were comparable to those in group 2. After the first injection of the toxin (alone), however, a marked erythema and some edema appeared over the remainder of the abdomen and particularly over that part into which the arsphenamine was injected in the previous experiment. In the other two guinea-pigs a less marked erythema appeared. These lesions subsided within two days.

The subsequent history in group 3 was one of diminishing reactions to the toxin, and when the test dose of neoarsphenamine was given there was but a small papular reaction in each guinea-pig. Here again the conclusion was drawn that after the early, possibly idiosyncratic, reactions, immunity developed to the toxin and that the degree of sensitization to the neoarsphenamine had greatly decreased during the experiment.

*Group 4.*—Twelve normal guinea-pigs were given toxin and neoarsphenamine with the technic outlined for group 1.

These guinea-pigs had increasing reactions to the first three of the injections and then decreasing reactions. The reactions to the test dose of neoarsphenamine



Included in the photograph are one of the guinea-pigs from group 2 and one from group 3. The thick, dark crusts on the right side of the abdomen represent the involuting reaction to the initial injection, the acute hemorrhagic and edematous lesions on the left side of the abdomen represent the reactions to the toxin alone, while within the broken lines the erythematous and slightly edematous flares can be clearly seen.

were small, and only seven of the twelve guinea-pigs reacted. The reactions produced small papules in every instance; in but one animal was there a surrounding erythematous flare the size of a nickel.

Toxin exhibited no significant effect in the cutaneous sensitization to neoarsphenamine in normal guinea-pigs.

*Group 5.*—This group of six normal guinea-pigs were given injections after the method suggested by Burky and with the knowledge that, according to Sulzberger,[4] sensitization would not occur. The toxin was mixed with the neoarsphenamine in the usual dosage and was injected intradermally at weekly intervals for five weeks.

Increasing local reactions were obtained to the first three injections and decreasing reactions to the last two. When the test dose of neoarsphenamine was given

alone, this group showed the fewest and the least marked reactions in the entire series. Only three of the six reacted, and these with minute papules.

No sensitization to neoarsphenamine was produced.

## COMMENT

Further experiments are now being made both with the animals previously used and with a new series of guinea-pigs. It is obviously impossible to draw conclusions from so small a group, and the experiment will be carried on throughout the year, various methods and different controls being used.

It is apparent that there was a curious decrease in sensitivity in the previously sensitized guinea-pigs throughout the experiment. Normal animals proved resistant to a brand of neoarsphenamine which in the earlier experiments was given a high sensitizing index. The addition of the highly potent toxin did not, with the exception of the early flare-up of old lesions, seem to have any augmenting influence in the production of hypersensitivity. The entire experiment suggested that some unknown factor was at work inhibiting the development of cutaneous arsenical idiosyncrasy.

The time of the experiment was from May 20 to July 5, and during that time the diet was kept constant, with large amounts of vitamin C. There may have been a slight increase in the amount of available sunlight, but this must have exerted a minor influence.

It is possible that sensitization to arsphenamine in guinea-pigs may, like allergy to tuberculin in human beings, undergo waves and changes with the seasons. In addition, different groups of guinea-pigs react differently even when the environment is a constant factor. The variation in the degree of sensitivity in a single group of guinea-pigs was another striking phenomenon.

Practically all dermatologists and syphilologists have noted the influence of infection on idiosyncratic and hyperallergic types of cutaneous eruption. The influence of intertriginous mycoses on the course of arsphenamine dermatitis has recently been commented on by Stokes and Kulchar.[8] It would appear that infections do predispose the organism to various idiosyncratic upsets and broaden the bases of existing allergies. The mechanism of this phenomenon is unknown. Burky [9] was under the impression that toxin has a general sensitizing influence which is intimately bound up with the production of specific hyperallergy and immunity. Hooker,[10] on the other hand, believed that

8. Stokes, J. H., and Kulchar, G.: Infection-Allergic Complex in Arsphenamine Dermatitic Reactions, with Special Reference to Dermatophytosis, Brit. J. Dermat. **46**:134 (March) 1934.

9. Personal communication to the author.

10. Personal communication to the author.

the action of the toxin is purely a locally irritating one and that any cutaneous irritant will serve the same purpose. The results of certain of the earlier experiments with guinea-pigs [1] have tended to confirm the latter impression.

## CONCLUSIONS

Different groups of guinea-pigs exhibited considerable variations in their ability to become sensitized to neoarsphenamine, these variations being independent of diet and of the brand of neoarsphenamine injected.

The age of the arsenical preparation may be a factor in the production of cutaneous hypersensitivity.

The Burnet staphylococcus toxin is highly lethal for guinea-pigs.

Continued injections of toxin intradermally in guinea-pigs produced increasing reactions, which indicated in part a developing sensitivity to the agar broth.

A degree of active immunity to staphylococcus toxin could apparently be developed in guinea-pigs.

The early injections of toxin seemed to activate the sites of old lesions due to arsphenamine.

Toxin (in this series) played no significant part in the production of cutaneous hyperallergy to neoarsphenamine in guinea-pigs.

Previously sensitized guinea-pigs may undergo marked variations in their cutaneous reactivity to neoarsphenamine.

There seemed to be an X factor, as yet unrecognized, which is essential for the production of cutaneous idiosyncrasy to neoarsphenamine in guinea-pigs.

# Case Reports

## SCLERODERMA CIRCUMSCRIPTUM EN COUP DE SABRE

JAMES HERBERT MITCHELL, M.D., CHICAGO

The occurrence of bandlike scleroderma circumscriptum of the forehead and scalp is sufficiently rare to make the recording of two cases of some interest. The first case was presented at the April meeting of the Chicago Dermatological Society in 1927.[1]

Fig. 1 (case 1).—Scleroderma circumscriptum en coup de sabre.

The patient was a nurse, aged 31, who had had a lesion on the right of the vertex for four years. The lesion began in the midline and gradually spread laterally and posteriorly. The hair fell out and did not grow in again. At the time of the onset the patient had lost weight but had since regained it. The basal metabolic rate had remained normal.

The lesion consisted of a fine, even band of waxy, hard scleroderma about 2.5 cm. in width from the hair line of the forehead half-way back to the crown. From the hair line to the right of the bridge of the nose there was a band of similar scleroderma the size of a pencil. The patient had an abscessed tooth on the upper right side which was to be extracted. After extraction of the tooth the patient left the city and has not been seen since.

1. Mitchell, J. H.: Scleroderma of the Scalp, Arch. Dermat. & Syph. **17:** 253 (Feb.) 1928.

The second case was presented at the March meeting of the same society in 1936.

The patient was a boy aged 16 years. The lesion had appeared twelve years before and was not preceded by any local disturbance so far as known. There had been no pain at any time. The right nares had always been more or less closed, and the patient had difficulty in blowing the nose. There was a moderate degree of exophthalmos. The patient's mentality was good, and he had no difficulty in keeping up with his work in the first year of high school. No radiotherapy had been received. The boy was taken to a radiologist about two years after the onset of the condition, and treatment with radium was advised. However, the fee was prohibitive and none was given.

Fig. 2 (case 2).—Scleroderma circumscriptum en coup de sabre.

The lesion, about 11 cm. in length, extended from the right supra-orbital notch upward to the right of the median line and for 3 cm. beyond the hair line of the forehead into the scalp. It was 2 cm. in width on the forehead, tapering to a point at the notch. The portion of the lesion on the scalp was firm and white, but the lower portion on the forehead was soft and somewhat pigmented. There was a marked depression in the portion on the forehead, and with the examining finger one obtained the impression of a loss of bone substance.

Dr. Nora Brandenburg examined the patient and reported as follows: "The patient had marked nasal obstruction due to a deflected septum and a very high palatal arch. The nasal obstruction apparently was due to a deflection and dislocation of the quadrilateral cartilage of the septum. The anterior border of the cartilage was completely dislocated out of the columella and crista incisiva to the left, causing narrowing of the left ala. A large left inferior turbinate bone also helped to obstruct the left vestibule. The deflection of the septal cartilage

was so great to the right that it completely closed the right vestibule by impinging on the right inferior turbinate bone. This point of contact between the cartilage and the turbinate bone was bathed in a mucopurulent discharge. Both maxillary antrums were indistinct on transillumination. The frontal sinuses were clear. Impacted cerumen was present in the right external auditory canal. There was marked thickening of the cartilage of the left auricle with angulation, causing narrowing of the external auditory canal. Impacted cerumen was present also in the left canal. Submucous resection and removal of the impacted cerumen from the ears would improve the patient's condition."

No roentgenogram or basal metabolic test had been made. The dentition was apparently entirely normal. The boy was one of a family of four children, aged 11, 16, 19 and 20. The Wassermann reaction was negative. The mother had had no miscarriage or stillbirth.

# Clinical Notes

## TINEA SYCOSIS OF THE UPPER LIP

THEODORE K. LAWLESS, M.D.,* CHICAGO

Since tinea sycosis of the upper lip alone seems to be a rare clinical entity, I wish to add the following case report to those recently recorded by Williams [1] and Davidson.[2]

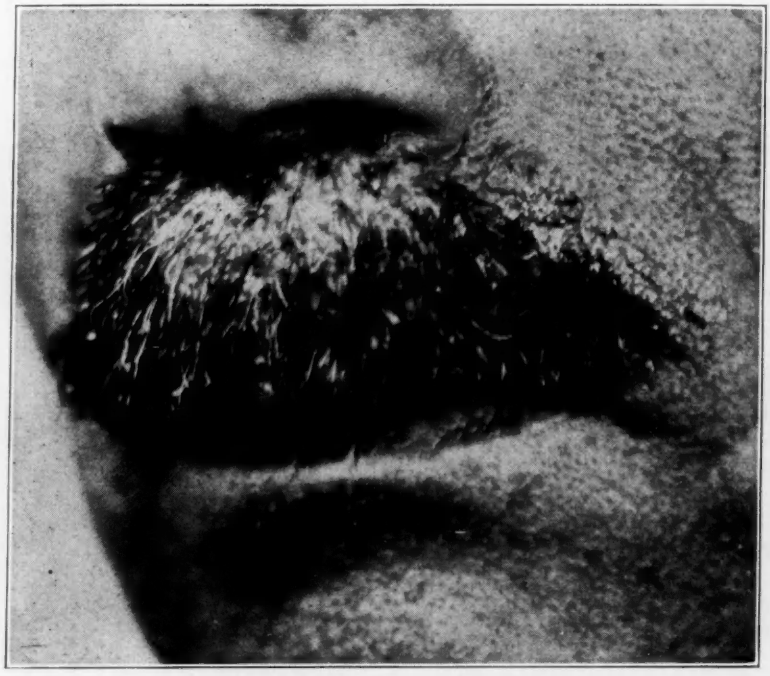


Fig. 1.—Tinea sycosis of the upper lip.

### REPORT OF A CASE

N. N., aged 50, unemployed for three years, was admitted to the dermatologic clinic, suffering from a swelling of the upper lip of three weeks' duration (fig. 1). In the center of the upper lip was a markedly inflammatory edematous lesion. The borders were well marginated, and the surface showed many large follicular

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* Elizabeth J. Ward Research Fellow.

1. Williams, C. M.: Tinea Barbae Involving the Upper Lip and Accompanied by Dermatophytid, Arch. Dermat. & Syph. **23**:213 (Feb.) 1931.

2. Davidson, A. M., and Dowding, E. S.: Tinea Barbae of the Upper Lip, Arch. Dermat. & Syph. **26**:660 (Oct.) 1932.

pustules, of which some were devoid of hair and some were pustular plaques. All of these lesions were deep-seated. The hairs in the involved area were easily removed.

A 20 per cent solution of potassium hydroxide determined the classification of the invading organism as Trichophyton endo-ectothrix. Cultures were made on maltose agar (French maltose and peptone). The original implantation of small pieces of hair showed pure culture after ten days. The growth was characterized by a smooth, round central cupula, with radiations from it resembling many closely

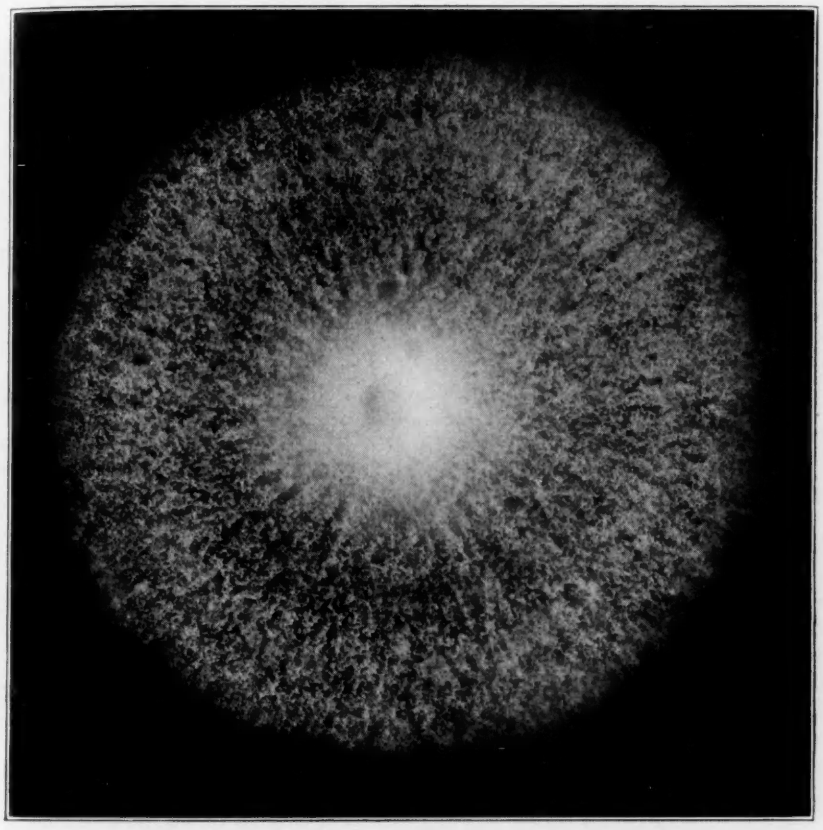

Fig. 2.—Petri dish culture of Trichophyton ectothrix-Trichophyton gypseum, Bodin (two weeks old).

formed spokes of a wheel. That part of the growth had definite thick and thin zones arranged centrifugally. The growth was coarse and pale yellow. The surface showed innumerable pearls of condensation. The outermost zone of the culture was composed of a fine, smooth, lacelike whitish zone. As the culture aged, the central portion was quickly covered by duvet, and the color deepened (fig. 2).

Microscopic examination of this culture showed the presence of pluriseptate spindles and aleuriospores (fig. 3). These characteristics, together with the

Fig. 3.—Hanging-drop culture, showing aleuriospores or meristem spores and club-shaped fuseaux.

macroscopic appearance, supported the diagnosis of Trichophyton ectothrix-Trichophyton gypseum, Bodin. An injection of 0.1 cc. of trichophytin intracutaneously gave a strongly positive reaction.

The treatment was as follows: Irregular and careless manual epilation was done by the patient. Six weekly intramuscular injections of a 1:50 dilution of trichophytin, beginning with 0.1 cc. and increasing by 0.1 cc. at each injection, were given, and then five injections of a 1:30 dilution, beginning with 0.4 cc. and increasing by 0.1 cc. at each injection. After the fourth injection had been given the lesions disappeared. More than a year afterward the patient was again seen. There had not been a recurrence of the condition.

## SUMMARY

A report is given of a case of tinea infection of the upper lip alone.

The diagnosis was confirmed by means of a potassium hydroxide preparation and by culture.

Treatment with trichophytin alone was successful.

# Minor Notes

## A SIMPLE PRACTICAL METHOD OF ADMINISTERING ARSPHENAMINE

A. B. Loveman, M.D., Louisville, Ky.

The advantages of arsphenamine over the other arsenical preparations are generally known. Many syphilographers fail to take advantage of its increased efficiency because of the difficulty of preparation and administration. This paper deals merely with the technic of administration. No noteworthy deviation from the usual technic of preparation is made, except that previously prepared commercial sodium hydroxide is employed.

The following apparatus, employed by me, can be modified to suit the individual administrator: (1) a graduated rubber-stoppered bottle (from 200 to 300 cc. capacity), (2) two glass tubes, one sufficiently long to reach the bottom, to act as a conductor of the fluid, and the other a relatively short one used to prevent the formation of a vacuum within the bottle, (3) one 10 to 12 inch (25 to 30 cm.) section of gum rubber tubing with a glass window, (4) one glass T-shaped bivalved adapter, (5) one 5 to 10 cc. eccentric tipped syringe and (6) one intravenous needle. The bivalved adapter is shown in figure 1. It is about 2 inches (5 cm.) long, and one end is so ground as to fit any size of needle. To the other arm is attached the piece of rubber tubing connected with the fluid which is to be injected. The adapter is so constructed that it permits the intake of fluids only through one arm and the exit only through the other. No manipulation of valves is necessary. The instrument is light, sterilizable and inexpensive and does not clog. When one pulls back the plunger to fill the syringe, a small amount of blood will be seen to enter the tip of the valve nearest the needle. This enables one to know at all times whether or not the needle is inserted into the vein of the patient. If there is not a flow of blood, the patient may be told to "make a fist" with the tourniquet applied. If the needle is in the vein, a small amount of blood will be forced back through the tip of the valve nearest the needle. In order to fill the system at the beginning of treatment, one should hold either the gloved finger or sterile gauze over this tip of the valve when pulling back the plunger. This allows the maximum of suction to take place.

I make no claim for originality of this set-up. I merely felt that a safe and simple method could be devised for administering arsphenamine in private practice and set out to develop one. The bivalved glass adapter was the solution. Although the method has its chief advantages for the administration of single doses, it can be used also for multiple doses. If this is done, additional adapters and rubber tubing should be on hand. This method is not an attempt to replace the gravity method for clinical administration, but I feel that it is a step forward in the administration of arsphenamine in private practice. Although I have given only between fifty and seventy-five injections with this technic, there have been no undesirable reactions, and I am still employing the original bivalved adapter. It is most important, however, that the injections be given slowly, at a rate of about 5 to 10 cc. per minute.

Among the advantages of such an apparatus are: (1) The old tubing reaction is practically eliminated or is certainly less likely to occur; (2) there is better regulation of the rate of flow of fluid; (3) it is easier to keep the solution

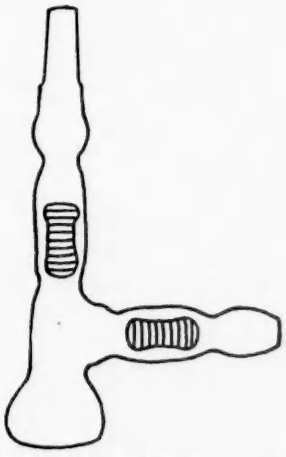

Fig. 1.—The adapter (actual size). The glass valves are shown by the shaded portion.

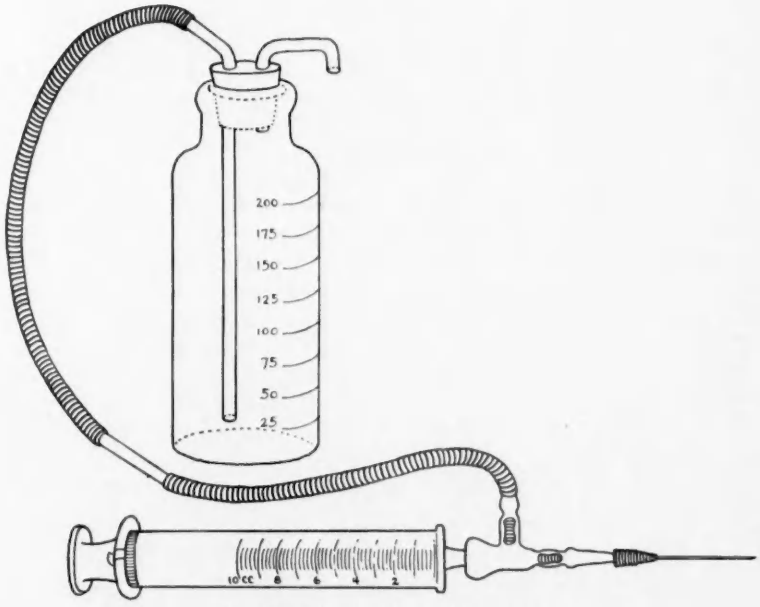


Fig. 2.—The complete apparatus.

at the proper temperature; (4) smaller needles (even hypodermic size if necessary) may be employed; (5) there is no need for elaborate apparatus, such as long tubing and large burets, etc.; (6) the method entails no great expense (the bivalved adapter costs $2), and (7) it works.

# Correspondence

## THE SO-CALLED LIBMAN-SACKS SYNDROME

*To the Editor:*—The article by Belote and Ratner in the April 1936 issue of the ARCHIVES (vol. 33, p. 642) has served to call to the attention of dermatologists the occurrence of a peculiar variety of endocarditis which is separate and distinct from that of rheumatic heart disease and subacute bacterial endocarditis (Libman and Sacks). It is, however, apparent that the subject of acute lupus erythematosus has fallen into a state of obfuscation. The discussions following the presentation of this paper are admirable, but the general effect is to leave the reader confused because of the differences in the point of view held by the various men. It is for this reason that I beg leave to make an attempt to clarify several important issues that have arisen. The implied query of Belote and Ratner of whether there is a disease peculiar to the Mount Sinai Hospital may be answered categorically in the negative. It is, however, not surprising that this question has arisen, because there are publications in which the impression is left with the reader that the general disease described is new or that it has not been recognized heretofore. I find myself in disagreement with this point of view for many reasons. It is likely that the syndrome reported by Belote and Ratner is none other than acute lupus erythematosus, as described originally by Kaposi (1869-1872). Credit is due Libman and Sacks for a masterly report on atypical verrucous endocarditis, a morphologic and clinical conception which attracted attention to a peculiar condition and which stimulated my interest in the subject of acute lupus erythematosus in 1930. It is my belief that this type of endocarditis, when encountered post mortem in acute lupus erythematosus, is part of the disease but that it is found only in a certain percentage of the cases, estimated roughly at from 30 to 50 (Gross). It is also encountered in patients presenting atrophic lesions of lupus erythematosus. However, certain qualifications must be made in order to appreciate the ramifications of this complex subject. 1. It is probable that the morphologic conception of this variety of endocarditis has not yet been fully defined or the precise limits established. 2. It is likely that a similar type of endocarditis may be found in several other obscure conditions, which may or may not be related to acute lupus erythematosus. 3. The condition is probably often missed at postmortem examination, particularly when lesions are present on, or are confined to, the mural endocardium, and it was overlooked in many institutions for a long time, until the classic report of Libman and Sacks appeared. In some cases it is probably labeled atypical rheumatic heart disease or subacute bacterial endocarditis, from which Libman and Sacks were the first to differentiate it on clinical and pathologic grounds. 4. Its presence can often be suspected when there is clinical evidence of pericarditis, as the two conditions frequently occur together; however, this rule admits of many exceptions. Diagnosis on the basis of valvular signs is unsatisfactory and resolves itself into a guess, which is as often wrong as right. 5. When organic physical signs of endocardial origin are noted, they are usually found to be attributable to concomitant valvular deformities. Whether these advanced changes are to be classified as old rheumatic cardiovalvular disease or whether atypical verrucous endocarditis can result in such alterations is still a moot point. The absence

of Aschoff bodies (Libman and Gross) constitutes definite evidence against the assumption that the patients afflicted with this disorder had died as a consequence of active rheumatic heart disease.

Thus, there occurs in a certain percentage of cases of acute lupus erythematosus a peculiar variety of endocarditis (valvular and mural) which can be classified as the Libman-Sacks type. The precise conception of this type of endocarditis and its variants awaits further clarification. It is my belief, also, that there is a group of cases which in the past have been correctly classified as instances of acute lupus erythematosus, and it is likely that Kaposi made a fundamental and brilliant contribution when he allied the condition in these cases to the atrophic variety of lupus erythematosus. In another place I shall bring together additional data that illustrate this relation. Regarding the tuberculous etiology of the acute variety of lupus erythematosus, which lends itself more readily to postmortem study from this point of view, it is interesting to note that the results of the more recent autopsies and investigations are confirmatory of the conclusions found in my paper on this subject. Although the French school is still convinced of the essential part played by tuberculosis in the causation of the condition, it is of great interest that Pautrier, one of the original and warmest advocates of this hypothesis, has recently become hesitant in regard to this view.

The remainder of this letter will be concerned with the following two fundamental questions:

1. Is the condition in the case recorded by Belote and Ratner a subvariety of the Osler "erythema group of diseases," and, if such is the case, what is the significance of this classification?

2. Is there evidence that the "lupus erythematosus-like" eruption of the Libman-Sacks syndrome is "erythema multiforme," representing a bacteria-free phase of a previous sepsis?

1. The conception proposed by Osler in a series of brilliant papers (1888 to 1916) is important for several reasons:

(*a*) The conception represented a distinct advance over that of Henoch and his pupils in that eruptions other than purpura were included in this group. In more modern terms, the preponderant number of his cases may be classed as instances of "capillary toxicosis" (Frank), a term which includes the Osler-Henoch-Schönlein group.

(*b*) Osler was among the first to imply correctly, on clinical grounds alone, that the visceral phenomena were probably analogous to the cutaneous manifestations from a clinical and a pathologic point of view. With the exception of a single postmortem examination, the organs (kidneys) of which were shown to him by MacCallum, he recorded no other pathologic data.

(*c*) Osler emphasized the features of abdominal crises and other gastrointestinal symptoms manifested in twenty-five of his twenty-nine cases, and he stressed the important surgical implications.

To Osler, therefore, one owes credit for the brilliant clinical conception of a generalized disease with varied cutaneous manifestations. However, in his last casuistic report there were included four cases in which the condition was unlike that in the others reported. I am concerned only with two of them, namely, case 19 and case 26, both of which were, in all probability, instances of acute lupus erythematosus. Without going into any great detail, it must be admitted that the group of cases recorded by Osler is heterogeneous, since it was the avowed purpose of Osler to seek similarities rather than dissimilarities. It seems advisable, on clinical and pathologic grounds as they are understood today, to separte these two instances with their peculiar and distinctive clinical pictures. Finally, it must

be emphasized that, as in these two cases in Osler's series, visceral crises in the sense of an acute abdominal condition necessitating surgical intervention are uncommon and do not form a distinctive part of the clinical picture that was so characteristically encountered in twenty-five of the twenty-nine cases recorded by Osler. It is my purpose to discuss elsewhere the few exceptions to this rule.

I therefore am unable to agree that the classification of the condition in the case reported by Belote and Ratner as a member of Osler's erythema group marks an advance in clinical conception.

2. The second question is divisible into three parts, each of which will be considered briefly and the details given elsewhere:

(*a*) The term lupus erythematosus-like implies a disease separate and distinct from the dermatologic lupus erythematosus and is, moreover, used by those who wish to deny the relation of the syndrome to that described by Kaposi or to atrophic lupus erythematosus. My observations are in disagreement with this point of view. The crux of the problem appears to rest on the contention that atrophy of the cutis is an essential requirement for the diagnosis of lupus erythematosus. Jadassohn, Brocq, Pernet and others had already stressed the point that there are cases of this disorder in which the element of atrophy is absent. My observations are in agreement with this point of view.

(*b*) The term erythema multiforme represents a veritable *caput mortuum* for a large number of dermatoses the classification of which is obscure. It will be shown elsewhere that there are at least four similar but distinctive varieties classified as erythema multiforme and that these may be differentiated from one another, in most instances, by careful attention to the morphologic attributes, the cutaneous clinical course and the internal medical aspects. That acute lupus erythematosus can manifest itself in the form of eruptive elements simulating "erythema multiforme" is well known, but it is my belief that such similarities, though occasionally striking, do not warrant inclusion of the conditions in a common group any more than the fact that the Henoch syndrome is occasionally diagnosed as ordinary appendicitis warrants the statement that they are related conditions. The term chronic erythema multiforme, so often used to designate acute lupus erythematosus, is, in my opinion, an unhappy expression employed by many to designate a variety of dermatoses.

(c) That acute lupus erythematosus (or the Libman-Sacks syndrome in the sense of Belote and Ratner) represents a bacteria-free phase of a previous sepsis is an attractive hypothesis, but everything about this view remains to be proved. As far as cases of acute lupus erythematosus are concerned, it may be stated that bacteriologic studies reveal the absence of known bacterial agents; the few positive results that have been obtained are susceptible of many other interpretations. It is true that the clinical picture reminds one of a severe infection or toxemia, but there is thus far no definite proof that the patients are at any time suffering from the effects of bacteremia attributable to known organisms (within the modern meaning of the term bacteremia), and the clinical picture is usually not that considered to be characteristic of ordinary "phlebitis sepsis." The demonstration of tubercle bacilli by the Löwenstein method of blood culture has been recorded, but the results published by various investigators are so discordant and the interpretation and evaluation of the positive findings so susceptible of criticism (Topley) that it must remain for the future to determine the value of the method in relation to the problem of lupus erythematosus.

HARRY KEIL, M.D., 509 Madison Avenue, New York.

# News and Comment

## PERSONAL

Dr. Edward R. Maloney has been appointed visiting dermatologist and syphilologist to Bellevue Hospital, taking the place of Dr. Mihran B. Parounagian, who has resigned because of ill health. Dr. Howard Fox has been appointed visiting dermatologist and syphilologist in charge of the combined services.

# Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

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SYPHILIS AND PRIMARY GLAUCOMA. WALTER BECKH, Am. J. Ophth. **18**:1129 (Dec.) 1935.

A series of 288 white patients and 77 Negroes with primary glaucoma formed the basis of the study. The incidence of syphilis was lower in both groups than in a similar number of patients admitted to the medical service. In the group of white patients with glaucoma the incidence of syphilis was lower than among white patients with cataract, but in the group of Negroes the incidence of syphilis was higher among patients with glaucoma than among those with cataract. A study of the age at onset of the glaucoma in the group of white patients showed that the syphilitic patients were three years older than the nonsyphilitic patients when the glaucomatous symptoms appeared, whereas among the Negro patients no such differences existed. In 18 of the 22 patients with syphilis, the disease was latent; 2 had asymptomatic neurosyphilis; 1 had demonstrable cardiovascular syphilis and another was suspected of having it. The syphilitic patients, treated with antisyphilitic as well as miotic therapy, responded somewhat less promptly than the nonsyphilitic patients, who were treated with miotics alone.

WIEDER, Milwaukee.

A GANGLIONEUROMA IN THE NECK OF A CHILD. J. MACFARLAND and S. W. SAPPINGTON, Am. J. Path. **11**:429, 1935.

The case described is one of well characterized ganglioneuroma. In this tumor, however, nerve cells in all stages of development from neuroblasts to ganglion cells occurred, and among them was a stroma made up of Schwann cells and nerve fibers. It occurred in the neck of a little girl, and the case seems to be the twelfth of its kind to be placed on record. Three years after operative removal the patient was living, and no return of the tumor and no metastases had occurred. Appended to the article are one hundred and forty-three references to the literature. FROM THE AUTHORS' SUMMARY. [AM. J. DIS. CHILD.]

THE VIRUS OF LYMPHOGRANULOMA INGUINALE. R. D'AUNOY, E. VON HAAM and L. LICHTENSTEIN, Am. J. Path. **11**:737, 1935.

Seven endemic strains of the virus of lymphogranuloma inguinale have been isolated and transmitted to animals. Intracerebral inoculation of infectious material produced typical meningo-encephalitis in the common marmoset whereas the rhesus monkey proved resistant to such inoculations. The virus could readily be transmitted to white mice, biweekly inoculation allowing upkeep of its maximal virulence. Emulsions of brain from infected monkeys and mice act excellently as stable and sensitive antigens for the specific diagnostic intradermal reaction of Frei. Twenty-eight per cent of infected guinea-pigs showed enlargement of the regional lymph glands with histologic lesions consistent with the disease. Experiments with sheep, chickens and frogs indicate that the virus can infect sheep, that its virulence can be preserved in the brains of chickens and that frogs cannot be infected.

THE CUTANEOUS GLOMUS AND ITS TUMOR—GLOMANGIOMA. O. T. BAILEY, Am. J. Path. **11**:915, 1935.

The cutaneous glomus is an arteriovenous anastomosis in the stratum reticulare of the cutis, which is homologous with the glomus coccygeum and several less important vascular structures. These have in common a specialized cell, which is

a modified smooth muscle cell with abundant nervous connections. The cutaneous glomus has an important function as an arteriovenous shunt in maintaining the body temperature and perhaps the blood pressure. From the cutaneous glomus, a tumor may arise which forms a subgroup of the hemangioma. The term "glomangioma" is suggested for it to indicate its derivation and character. Glomangioma appears as a small bluish nodule on an extremity or an adjacent portion of the shoulder girdle. Very frequently it is located in the nail bed. Microscopically the tumor is composed of cells identical with those in the walls of the normal cutaneous glomus and its homologue. Nerve trunks are numerous in the connective tissue about the tumor, and nerve filaments pass among the glomus cells in large numbers. Occasionally elongate smooth muscle cells are seen either in solid masses or adjacent to vascular lumens. The glomangioma represents the overgrowth of the entire arteriovenous anastomosis, and the cells show a twofold differentiation: First, the elongate smooth muscle cells lose all myofibrils, while the reticulum investing them becomes much coarser and stains intensely with collagen stains. Second, the periglomic nerves grow into the tumor, and their terminal filaments end about the differentiating smooth muscle cells with the interposition of nerve endings. These two processes result in the formation of the glomus cells and are apparently interdependent. The tumor is associated clinically with severe radiating pain of neuralgic type. In character and distribution this has many similarities to the response of the normal glomus to much greater stimuli of the same character. Glomangiomas thus represent functionally as well as morphologically organoid overgrowths. Glomangiomas do not become malignant. Local excision gives complete and permanent relief from symptoms.

FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.]

RADIUM DOSAGE AND TECHNIQUE IN BENIGN LESIONS OF THE SKIN. HOWARD MORROW and LAWRENCE R. TAUSSIG, Am. J. Roentgenol. **32**:735 (Dec.) 1934.

The limitations of the use of radium due to the danger of late sequelae, such as telangiectasia, atrophy, keratosis and malignant growth, are outlined, and a method of guarding against such sequelae is given. Roentgen therapy has proved superior to radium in the treatment of many diseases, such as psoriasis, lichen planus, eczema, etc. The authors outline the treatment and give the dosages of radium for the following conditions: congenital anomalies, such as vascular and fleshy nevi, and acquired conditions, such as keloid, verruca, synovial cyst and epulis.

SQUIRES, Chicago. [AM. J. DIS. CHILD.]

CUTANEOUS TUBERCULOSIS AND GENERAL MEDICAL DIAGNOSIS. FRANCIS E. SENEAR, Ann. Int. Med. **8**:1274 (April) 1935.

In this article, which deals with diseases of the skin bearing a relationship to tuberculosis, Senear states that erythema nodosum occurring in children is frequently of tuberculous origin. It tends to occur early in the course of tuberculous disease and necessitates prolonged convalescence and careful observation for at least six months.

Erythema nodosum of tuberculous origin is apt to occur in unusual locations and exhibits a greater tendency to localize on the posterior aspect of the legs. The nodules are smaller and tend to be less numerous and acute, and the process as a whole is less active than when the disorder is due to other causes.

It is also suggested that erythema multiforme may be of tuberculous origin in a small proportion of cases.

READING, Galveston, Texas. [AM. J. DIS. CHILD.]

THE ANORECTAL PHASE OF LYMPHOGRANULOMA INGUINALE. A. W. MARTIN MARINO, Ann. Surg. **102**:1086 (Dec.) 1935.

Three cases of lymphogranuloma inguinale, two occurring in white women and the third in a Negress, are described. In one of these patients, a white woman, the process had caused the entire rectum and the sigmoid and descending portions

of the colon to be stenosed owing to infiltration of all the coats. In the three patients there were, respectively, rectal stricture with perianal fistula, rectal stricture with perianal elephantiasis and rectal stricture with elephantiasis complicated by perianal fistula. The three patients received several courses of antimony and potassium tartrate intravenously without appreciable benefit.

WIEDER, Milwaukee.

RELATIONSHIP OF PELLAGROUS DERMATITIS TO SUNLIGHT. T. D. SPIES, Arch. Int. Med. **56**:920 (Nov.) 1935.

In this study pellagrins receiving a diet of 2,900 calories but low in pellagra-preventive substances were exposed to radiation from a quartz mercury vapor arc lamp, areas of skin that appeared normal and some pellagrous lesions being irradiated.

The effect of dermatitis, pigmentation and desquamation was produced on the normal appearing skin, but the reaction could not be diagnosed as pellagrous. The pellagrous lesions became more deeply pigmented but the irradiation did not prevent their healing.

Normal persons and pellagrins were exposed in an identical manner to sunlight, but the resulting reaction showed no difference in intensity or character.

Four patients who had been cured of pellagra were given a deficient diet and kept from exposure to sunlight. Within six weeks the characteristic dermal and other changes developed.

Spies considers that pellagra should be regarded as a systemic disease which is the real cause of pellagrous dermatitis, but he believes that under certain conditions sunlight may act as the precipitating irritant in the production of the cutaneous lesions.

DIFFERENTIAL DIAGNOSIS OF RUBELLA: USE OF THE SCHILLING DIFFERENTIAL LEUKOCYTE COUNT. C. M. MACBRYDE and C. M. CHARLES, Arch. Int. Med. **56**:935 (Nov.) 1935.

Serial differential blood counts by the Schilling method were made by MacBryde and Charles in thirty cases of rubella. The authors believe that these counts differed significantly from the counts obtained in other conditions—chiefly measles, scarlatina and toxic rashes—which might be confused with rubella.

JAMIESON, Detroit.

AN ATYPICAL FAMILIAL ENDOCRINOPATHY IN MALES WITH A SYNDROME OF OTHER DEFECTS. WILLIAM ANTHONY REILLY, Endocrinology **19**:639 (Nov.-Dec.) 1935.

Reilly reports three cases of a syndrome first described by Hunter in 1917. It is familial, occurs only in male children and is characterized by optic neuritis, a typical physical appearance due to similar facies, changes in the bones and joints, hepatosplenomegaly and coarseness, dryness and thickness of the hair.

In the author's first case the skin was thick, coarse and freckled and the tongue was enlarged and rough. At autopsy areas of degeneration and necrosis were observed in the anterior lobe of the pituitary body. There was also mild hyperplasia of the thyroid gland.

In the second case there was a similar clinical picture, but a biopsy of the skin showed only a mild chronic nonspecific dermatitis. Reilly does not mention results of stains for mucin.

In the third case the skin and hair were dry and coarse, and there was increased growth of hair on the face, arms and eyebrows.

Reilly states that although the facies, tongue, hair, texture and appearance of the skin suggested hypothyroidism and other signs suggested hypopituitarism, many features of the syndrome could not be explained merely on a basis of endocrinopathy.

LYNCH, St. Paul.

THE INFLUENCE OF LATENT SYPHILITIC INFECTION ON THE REACTION OF THE RABBIT TO THE BROWN-PEARCE TUMOR. P. D. ROSAHN, J. Exper. Med. **62:** 213 (Aug.) 1935.

As a result of this experimental work Rosahn found a lower mortality rate in the combined group (fifty rabbits of five breeds) than in the control group of normal nonsyphilitic rabbits. This was also true for each individual breed.

Relative resistance of the different breeds to the Brown-Pearce tumor was not altered by the latent syphilitic infection.

There was also found a high correlation between the resistance of the breed to infection with Spirochaeta pallida and the resistance to the Brown-Pearce tumor.

CUTANEOUS REACTIVITY OF IMMUNE AND HYPERSENSITIVE RABBITS TO INTRADERMAL INJECTIONS OF HOMOLOGOUS INDIFFERENT STREPTOCOCCUS AND ITS FRACTIONS. C. MCEWEN and H. F. SWIFT, J. Exper. Med. **62:**573 (Oct.) 1935.

McEwen and Swift inoculated rabbits intradermally with a soluble streptococcus protein after having immunized them intravenously with the same protein. The result was an immediate anaphylactic type of dermal response. However, in the rabbits immunized by intracutaneous inoculation of the intact organism and subsequently tested in the same manner by intradermal inoculation a delayed type of response was elicited.

JAMIESON, Detroit.

INFANTILE ECZEMA. W. O. COLBURN, Nebraska M. J. **20:**21 (Jan.) 1935.

Cutaneous tests are not recommended for the determination of the offending protein in infantile eczema. The results are unreliable in children less than 6 months of age. Desensitization by subcutaneous use of the mother's milk, which is boiled in a water bath for three minutes is recommended. The doses start with 1 minim (0.06 cc.) and are increased 1 minim every other day until 4 minims (0.24 cc.) is given; they are then given twice weekly and are increased 1 minim for each dose until from ten to fifteen doses have been given, depending on the results.

HAMILTON, Omaha. [AM. J. DIS. CHILD.]

CHRONIC ATROPHIC DERMATITIS OF THE VULVA. F. L. ADAIR and M. E. DAVIS, Surg., Gynec. & Obst. **61:**433, 1935.

The descriptive term employed here is preferable to any of the many names hitherto proposed because it indicates the nature of the entire process rather than emphasizes only certain phases of the condition. Among patients with gynecologic disorders seen by the writers the incidence of the lesion at one stage or another was 0.24 per cent. It is a progressive disease and, unless vulvectomy is performed, leads to carcinoma in more than half of the cases. The three stages of the lesion are excellently depicted in colored plates.

HUNTER, Portland, Ore. [ARCH. PATH.].

STUDIES IN CHEMOTHERAPY: XII. THE DIFFUSIBILITY OF THE AROMATIC ARSENICALS INTO ERYTHROCYTES AND THE ACTION OF THE LATTER ON THE PENTAVALENT ARSENICALS. E. M. LOURIE, F. MURGATROYD and W. YORKE, Ann. Trop. Med. **29:**265 (July) 1935.

Lourie, Murgatroyd and Yorke found that when red blood cells were suspended in a solution of tryparsamide in Ringer's solution with glucose a certain amount of the drug rapidly passed into the red cells. The laked red cells, after separation from the drug solution, were powerfully trypanocidal.

If the red cells were suspended for twenty-four hours in the solution containing tryparsamide the laked blood cells were found to contain approximately twice as much tryparsamide as after a fifteen minute exposure. However, if these cells were treated by washing, less of the drug could be recovered than after the shorter exposure; this suggested that some of the drug is more firmly bound to the substance of the red cells during the longer exposure.

JAMIESON, Detroit.

CUTANEOUS MYIASIS IN INFANTS. N. SILVERTHORNE and A. BROWN, Arch. Dis. Childhood **9**:339 (Dec.) 1934.

Three cases of cutaneous myiasis produced by larvae of Wohlfahrtia vigil (Walker) in infants are reported. The larvae are discharged on the surface of the patient's skin by the gravid fly. The larvae quickly migrate to areas where there are folds and burrow into the subcutaneous tissue, producing an inflammatory reaction. The lesions disappear after the larvae are removed, either by forceps or by squeezing. In the three cases reported, larvae removed from the lesions of the skin were reared to adult flies. The lesions occurred in healthy infants sleeping outdoors during June.

PAPULAR URTICARIA (LICHEN URTICATUS). B. C. TATE, Arch. Dis. Childhood **10**:27 (Feb.) 1935.

A thorough investigation, mainly of the etiology, of this cutaneous disease is reported, with the following conclusions:

Papular urticaria is a definite and distinct syndrome, distinguishable from urticaria and from Hebra's prurigo. It is a manifestation of allergy. It is essentially a disorder of the first four years of life. It is aggravated by heat and by a diet containing too much carbohydrate. Digestive disorders, teething and mild febrile disturbances probably predispose to papular urticaria, but such conditions are of minor importance in the etiology. Rickets plays no part. There is no satisfactory evidence of any underlying diathesis. The exciting agent is not a food but something connected with the home environment of the patient, the precise nature of which remains obscure. The agent is not bedding or clothes, but it can be carried on these articles. It is not vermin or an antigen derived from human beings or domestic animals. Sensitivity to house dust has not been definitely excluded.

KELLY, Milwaukee. [AM. J. DIS. CHILD.]

PRESENCE OF HEMOLYTIC AND OTHER STREPTOCOCCI ON HUMAN SKIN. L. COLEBROOK, W. R. MAXTED and A. M. JOHNS, J. Path. & Bact. **41**:521, 1935.

Hemolytic streptococci of the kind usually associated with human puerperal infections (Lancefield's group A) were not found on the perineal and perianal skin of 160 women attending an antenatal department, and the risk of such streptococci being conveyed to the genital tract from the feces is considered to be remote. Group A hemolytic streptococci were isolated from the hands of 7 of 181 normal persons (3.8 per cent). It seems probable that they were derived from the respiratory tract. Treatment of the mother's hands during labor by an antiseptic is advocated. Nonhemolytic types of streptococci (chiefly Streptococcus viridans) were found on nearly all the hands investigated but not on the skin of the interscapular region.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

THE ULCER SYNDROME IN TROPICAL AFRICA. A. A. F. BROWN, J. Trop. Med. **38**: 157 (July 1) 1935.

Brown classifies ulcers into groups A, B and C. Ulcers of group A are about the same all over the world; they are due to trauma, scabies, yaws, etc. Ulcers of group B are typical phagedenic ulcers, frequently arising from a vesicle. Those of group C are clinically identical with those of group B, but they are due to trauma and become phagedenic later on.

He analyzes the observations on ulcers during a five year period and expresses the belief that a strong correlation exists between Bacillus fusiformis and Spironema and the phagedenic type of ulcer. In the laboratory it was impossible to obtain a pure culture of B. fusiformis alone.

Clinically ulcers were phagedenic and nonphagedenic. Forty-six and one-tenth per cent of the ulcers in Brown's series failed to reveal B. fusiformis.

In a series of 423 males examined bacteriologically 53.9 per cent showed B. fusiformis and/or Spirochaeta Schaudinni, and in 89 per cent of these the ulcers were phagedenic. The presence of these organisms in a nonphagedenic ulcer indicated a change in character to the phagedenic form. (The article is to be continued.)

THE ULCER SYNDROME IN TROPICAL AFRICA. A. A. F. BROWN, J. Trop. Med. **38**:170 (July 15) 1935.

In this instalment the writer discusses several questions regarding the pathogenicity of Bacillus fusiformis and Spironema. It is difficult to determine whether the phagedenic ulcers in question form a suitable medium for the organisms to develop or whether the organisms themselves produce the change from the traumatic to the phagedenic type of ulcer. Lesions of the mucous membranes due to Vincent's bacillus usually responded well to arsenic therapy while the tropical phagedenic ulcers did not. The vesicles which usually preceded the ulcers did not contain B. fusiformis. Inoculations of animals likewise gave negative results. Phagedenic ulcers which did not contain B. fusiformis were of a different type.

Brown suggests that B. fusiformis and Spironema may be the cause of phagedenic ulcer but that it is difficult to prove this point, as pure cultures of the organisms have not been obtained.

Ulcers were found slightly less often in female patients. Dietary changes were believed to be partially accountable for variations in the incidence according to tribes. Ulcers showed no improvement under treatment with arsenic, bismuth or mercury unless they were definitely of the syphilitic or yaws type.

The treatment of patients with ulcers was complicated in many instances by the presence of endoparasites, malarial organisms, hookworms, etc. (The article is to be continued.)

THE ULCER SYNDROME IN TROPICAL AFRICA. A. A. F. BROWN, J. Trop. Med. **38**:187 (Aug. 1) 1935.

Treatment of ulcers consists of scraping, if necessary, of ordinary local treatment and of a standard hospital diet. If satisfactory progress does not follow in two or three weeks, calcium chloride is given intravenously in doses of 15 grains (0.97 Gm.) in 10 cc. of distilled water once or twice daily. If results are still unsatisfactory after ten days, parathyroid extract is given orally. The average duration of treatment is about six weeks.

The results of this treatment in the series of cases observed by the author indicate that a definite benefit was derived from the intravenous administration of calcium chloride. Approximately 30 per cent of the patients with phagedenic ulcers had a low calcium level. The level for phosphorus varied from a low value of 1.8 mg. to a high value of 11.2 mg. per hundred cubic centimeters of blood serum. Ulcers were not commonly found in members of tribes who consumed flesh, beans and ground nuts. It appears from this that the diet is largely responsible for the development of these ulcers.

JAMIESON, Detroit.

STILL'S DISEASE WITH ERYTHEMA MULTIFORME. DONALD PATERSON, Proc. Roy. Soc. Med. **28**:157 (Dec.) 1934.

A case of this condition in a boy aged 6½ years is reported. The history, the results of physical and roentgen examination and the treatment are given. The dermatologist reported that the cutaneous lesions were those of erythema multiforme, probably evidence of a former streptococcic infection.

WILLIAMSON, New Orleans. [AM. J. DIS. CHILD.]

CALCINOSIS. W. D. W. BROOKS, Quart. J. Med. **3**:293 (July) 1934.

The literature concerning calcinosis is reviewed. Brooks then presents the results of his own experimental study concerning the calcium and phosphorus balance in a case of calcinosis in a girl aged 15 and also in a case of scleroderma in a woman aged 41. In the girl, pathologically high levels of serum calcium, plasma inorganic phosphate and plasma phosphatase were maintained over a long period, whereas these values were normal in the patient with scleroderma. The calcium metabolism in the girl was restored to approximate balance by the administration of di-sodium hydrogen phosphate. The author suggests that in calcinosis a local tissue change, not yet clearly understood, results in localized damage to fibrous tissue and that when calcification occurs in these areas an abnormality of calcium and phosphorus metabolism may also occur. Brooks expresses the belief that the type of lesion in scleroderma does not necessarily produce abnormal changes of the calcium and phosphorus metabolism.

BRADFORD, Rochester, N. Y. [AM. J. DIS. CHILD.]

OBSERVATIONS ON SYPHILIS OF THE PLACENTA. M. BRINDEAU and Y. MANOUÉLIAN, Bull. Soc. de pédiat. de Paris **31**:441 (Nov.) 1933.

The placenta of a 20 year old woman, delivered of a syphilitic infant, had the gross appearance of syphilitic involvement. It was studied histologically by a silver impregnation method for the identification of Spirochaeta pallida. The striking observation was made that the organisms were few in the placental tissue and in the blood but that in the walls of the tiny venules they were unusually plentiful, forming interlacing networks in places. While some of the spirochetes were typical in morphologic characteristics, many showed various stages of change, assuming ringlet and crown shapes and losing the appearance of spirals. The organisms were chiefly seen in phagocytic cells. Spirochetes were also noted in the cutaneous lesions of the infant. Sections of the umbilical cord showed many organisms in Wharton's jelly, and although few could be seen in the blood which filled the vein, they occurred for the most part within phagocytes.

A CASE OF CYTOSTEATONECROSIS IN A NEW-BORN INFANT. L. BABONNEIX and DIRIART, Bull. Soc. de pédiat. de Paris **32**:519 (Nov.) 1934.

An infant, 3 weeks old, presented marked induration of the skin over the entire back, which was violet-colored. The skin was ligneous in consistency and could not be creased or raised from the deeper tissue. This condition did not seem to disturb the infant, as he thrived well. There was a history of trauma immediately after birth, as the obstetrician spanked him repeatedly on the back over a period of twenty minutes on account of marked asphyxia. It took about a month for the skin to assume its normal characteristics. The abnormal condition is due to necrosis of the subcutaneous adipose tissue.

VARIOUS CASES OF ACRODYNIA AND THE TREATMENT. P. DUHEM and ERNEST HUANT, Bull. Soc. de pédiat. de Paris **32**:527 (Nov.) 1934.

Six cases of acrodynia in children, ranging in age from 1 to 14 years, are described. Cases of hypotonicity for which no definite cause can be found should suggest the possibility of acrodynia. The first improvement which generally takes place is to be observed in the tone and disposition; this occurs long before any marked amelioration of the trophic disturbances becomes evident. Investigation of the neurovegetative responses, such as the oculocardiac reflex and the cardiac acceleration, after the subcutaneous injection of a solution of epinephrine is advised, both as an aid to diagnosis and a guide in physical therapy. It is believed that the most probable etiologic factor in this disease is neuro-endocrine.

PRIMARY TUBERCULOUS CUTANEOUS INOCULATION AND REGIONAL ADENITIS TREATED SURGICALLY. M. COFFIN, Bull. Soc. de pédiat. de Paris **32**:535 (Nov.) 1934.

In a girl, 7 years old, inguinal adenitis developed after a wound on the knee, which became infected and left a violet paper-like scar. A number of inguinal glands were originally involved, but the condition subsided in all except one, in which it progressed until the tissue broke down. The glands were excised, as well as the area of unhealthy skin. Histologically tubercles were observed in the glands, and bacilli were demonstrated in them. The skin showed typical epithelioid and giant cells with involvement of a sweat gland. The child had been in contact with the father, who had tuberculosis. The reaction to the tuberculin test was positive. It is considered that in this case there was a primary tuberculous lesion of the skin, the bacilli having entered by way of a wound, and that the inguinal glands became involved by extension up the leg of bacilli through the lymphatic channels. Primary tuberculosis of the skin is serious in infants, who may succumb to the infection, but in older children the prognosis is much better. When the skin is secondarily involved by tubercle bacilli which originate in other foci in the body, the lymph glands in the region of the infected skin do not usually caseate.

BENJAMIN, Montreal, Canada. [AM. J. DIS. CHILD.]

FINDING OF HEMISPORA STELLATE IN RINGWORM OF THE SCALP. M. PAVIA, Riv. di clin. pediat. **33**:144 (Feb.) 1935.

In cultures of material taken from the lesions of ringworm of the scalp in a girl aged 7 years, the author was able to identify Hemispora stellata Viullemin in pure culture; later cultures yielded Achorion Schoenleinii. It is unusual to find Hemispora stellata as the etiologic agent in such lesions of the scalp.

GERSON-HERRMANNSDORFER-SAUERBRUCH DIET IN THE TREATMENT OF CHILDHOOD TUBERCULOSIS. A. GOLIN and R. DEMENIGHINI, Riv. di clin. pediat. **33**:257 (March) 1935.

Thirty children between the ages of 3 and 9 years, having various types of tuberculosis, were given a diet patterned after those of Gerson, Herrmannsdorfer and Sauerbruch. The diet is definitely low in sodium chloride and high in vegetables and fruits. A sample diet for a 6 year old child weighing 43 pounds (19.5 Kg.) contained the following foods:

Milk, 500 Gm.; meat, 80 Gm.; vegetable purées, 100 Gm.; raw or steamed greens, 100 Gm.; cooked fruit, 100 Gm.; raw fruit, 100 Gm.; macaroni, 20 Gm.; bread, salt-free, 40 Gm.; butter, 20 Gm.; cod liver oil, 40 Gm., and olive oil, 20 Gm.

The values of the diet were as follows: protein, 2.6 Gm.; fat, 6 Gm., and carbohydrate, 7.4 Gm., per kilogram of body weight.

Sixteen of the thirty children did excellently, and nine others, fairly well, when they were fed the diet; it led not only to improved nutrition but to clinical improvement. The other five children did not do well clinically, although several showed a gain in weight and an increase in the hemoglobin concentration.

HIGGINS, Boston. [AM. J. DIS. CHILD.]

HEMANGIOMAS AND LYMPHANGIOMAS: RESULTS OF TREATMENT. G. GERLACH, Beitr. z. klin. Chir. **159**:129, 1934.

Gerlach studied all the cases observed by him between 1918 and 1933 in order to learn what method of treatment was preferable not only from the standpoint of elimination of the condition but also from that of the cosmetic results.

Eighty-four patients were treated, and fifty-one were followed up. Included among these were seventy-one patients with hemangioma, twelve with lymphangioma and one with a combination of both conditions. The hemangiomas were

treated as follows: Thirty-four were excised, twenty-nine were treated with radium, two were needled with magnesium, two were punctured, two were treated with injections of alcohol and with radium and one was excised and treated with radium. Treatment of the lymphangiomas was as follows: Seven were excised, two were treated with radium, one was needled with magnesium and two were not treated. The lesion which was a combination of hemangioma and lymphangioma was excised.

Total extirpation left a small scar which faded in late years. Bad results were seldom seen. Treatment with radium gave good results, but from the cosmetic standpoint the results were not as good as those following surgical intervention—scars were more prominent. Pigmentation around the periphery was more obvious in the patients treated with radium. In several cases in which the involvement was severe good results were also obtained by needling with magnesium.

RUBIN, Boston. [AM. J. DIS. CHILD.]

THE PROPHYLACTIC EFFECT OF A SOLUBLE PREPARATION OF ARSPHENAMINE IN EXPERIMENTS WITH ANIMALS. RICHARD WAGNER, Dermat. Wchnschr. **99**: 1609 (Dec. 15) 1934.

The prophylactic activity of 3, 4′ di-acetyl amino-4-hydroxyarsenobenzene-2-sodium glycocholate suitable for intramuscular injection was tested on a series of rabbits. The Nicholas strain of Spirochaeta pallida was used, and the inoculations were made by scarification of the scrotum. The manufacturers stated that the therapeutic dose of the preparation for rabbits was from 5 to 10 mg. per kilogram. Doses of 2.5, 5 and 10 mg. per kilogram given two hours before or two hours after inoculations did not prevent the formation of the chancre. It required a dose of 20 mg. per kilogram to prevent development of the chancre.

TREATMENT OF LUPUS ERYTHEMATOSUS WITH ESTERS OF CHAULMOOGRA AND HYDNOCARPUS OIL. SVEND LOMHOLT, Dermat. Wchnschr. **101**:817 (July 6) 1935.

Lomholt reports the results of treatment of thirty-one patients with lupus erythematosus with esters of chaulmoogra and hydnocarpus oil. A brief report of cases and a number of photographs made before and after treatment are given. The drug was given either intravenously in doses of from 1 to 2 cc. in 9 cc. of an 8 per cent solution of alcohol or intramuscularly in doses of from 1 to 2 cc. with a proprietary brand of ethyl aminobenzoate either daily or two or three times a week. In general Lomholt prefers the intravenous route, though the results were apparently the same. Intravenous injections frequently caused brief periods of headache or shortness of breath and occasionally a rise in temperature. An average of twenty injections were given each patient. Of the group of patients forming the basis of this study, eleven were cured, twelve much improved, seven somewhat improved and one unimproved. Finsen light was also used in some instances.

THE HISTOGENESIS OF NEVUS SYRINGOCYSTADENOMATOSUS PAPILLIFERUS. J. DÖRFFEL, Dermat. Wchnschr. **101**:855 (July 13) 1935.

A 30 year old woman presented a warty growth in the right parietal region which had been present for at least ten years and had increased slowly in size. Clinically it was a superficial epithelioma or a nevus of a sebaceous sudoriferous gland. Histologic examination showed a sweat gland-like epithelial hyperplasia appearing to arise from the basal layer of the epidermis. Some areas were papillary; others presented the picture of an intra-epidermal epithelioma. Plasma cells were abundant in the infiltrate, and there were also numerous mast cells. Dörffel is of the opinion that these observations bear out his theory of the pluripotency of epithelial cells.

A Simplified Staining Method for Demonstrating Fungi in Scales and Hair. J. Alkiewicz and W. Górny, Dermat. Wchnschr. **101**:1034 (Aug. 24) 1935.

The authors found the following method satisfactory in staining fungi in scales and hair: The material is fixed and fastened to the slide by heating a few moments over a flame in a solution consisting of ten parts of a dilute solution of formaldehyde (4:10) and a hundred parts of alcohol. It is then stained in one part of cresyl violet (Grübler) and a hundred parts of 0.9 per cent solution of sodium chloride for about five seconds while being warmed gently. The preparation is then dried carefully with filter paper and mounted in oil of cloves.

Taussig, San Francisco.

The Demonstration of Thallium in the Tissues. J. Schneller, Deutsche. Ztschr. f. d. ges. gerichtl. Med. **25**:222, 1935.

Thallium was demonstrated spectroscopically in the urine and stool of a woman three and one-half months after she had ingested 0.37 Gm. of the poison. It could not be detected by ordinary means. This slow excretion was confirmed in dogs and guinea-pigs poisoned with thallium. Tests showed its presence in the bones long after all traces of the metal had disappeared from other organs.

Rukstinat, Chicago. [Arch. Path.]

Treatment of Ninety-Six Patients with Neurosyphilis by Active Immunization with Nonpathogenic Cultures of Spirochaeta Pallida. L. Benedek, Monatschr. f. Psychiat. u. Neurol. **88**:1 (Feb.) 1934.

Benedek treated ninety-six patients suffering from neurosyphilis with injections of Hilgermann's cultures of living but avirulent spirochetes. There were fifty-six patients with dementia paralytica and thirty-three with tabes. The group included elderly persons who were in poor physical condition. There was no evidence to suggest that the transfer of the avirulent strain of spirochetes to the human organism could activate the spirochetes and lead to a generalized or localized superinfection. However, focal nervous symptoms were sometimes increased temporarily. Thus, all but six of the patients with tabes showed an increase of such symptoms as lightning pains, gastric crises and paresthesia during the course of treatment. As a rule, a slight to moderate rise of temperature and moderate leukocytosis occurred. Local cutaneous or connective tissue reactions were noted in eleven patients after repeated injections of the vaccine. The formation of abscesses was observed in three patients. This was probably due to contamination of the cultures with other bacteria. Seventy-five patients had previously received some form of treatment, but only eight had shown improvement. This included two patients who had complete remissions. In sixty-nine cases the cultures of spirochetes were given in conjunction with other types of therapy. The latter consisted of one course of treatment with antisyphilitic drugs in thirty-one of these cases. Fifty-five patients showed improvement during or shortly after the administration of the vaccine; twenty-four patients showed no change, and ten became worse. One patient died during treatment, but necropsy disclosed a neurinoma of the cerebellopontile angle as the cause of death. It was possible to follow seventy-five patients for approximately from two to three years. Complete remission had occurred in thirteen, considerable improvement in twelve and slight or moderate improvement in fifteen. Sixteen members of the group had died. Better results were noted in the group with tabes than in that with dementia paralytica, 54.5 per cent of the patients in the former and 25 per cent of those in the latter group showing improvement.

The serologic reactions were studied in fifty-one cases. The Wassermann reaction of the blood became negative in four cases and that of the spinal fluid in seven cases. The colloidal gold reaction showed improvement in 49 per cent of the group, and the cell counts were diminished in 52.9 per cent. It was not

possible to determine whether there was any correlation between clinical and serologic changes, owing to the fact that the lumbar punctures were performed without regard to the clinical condition of the patients. A scrutiny of the results obtained in patients treated solely with injection of spirochetes leads Benedek to conclude that vaccine therapy is as efficacious as other forms of treatment. The results are favorable enough to suggest that with further development of the method still greater success in treatment may be obtained.

ROTHSCHILD, Foxborough, Mass. [ARCH. NEUROL. & PSYCHIAT.]

CONGENITAL ICHTHYOSIS. W. COURTIN, Ztschr. f. Kinderh. **55**:384 (Sept.) 1933.

Courtin reports the case of an infant born 4 weeks prematurely, with no family history of disease of the skin, who from the first day of life showed cornification of the skin. The picture was that of the congenital ichthyosiform erythroderma described by Brocq. The author could find no etiologic factor for the disease. He excluded syphilis.

LEVINSON, Chicago. [AM. J. DIS. CHILD.]

ANIMAL EXPERIMENTATION AND THE VIRUS OF LYMPHOGRANULOMA INGUINALE. I. TOYAMA, M. HASEGAWA and T. ICHIKAWA, Jap. J. Dermat. & Urol. **37**:351 (March); **38**:21 (Aug.) 1935.

The authors report the results of experiments with the virus of lymphogranuloma inguinale on monkeys and guinea-pigs (first communication) and on squirrels, Eutamia orientalis (second communication).

The material used was the pus or the macerated material from glands of patients with clinically proved lymphogranuloma inguinale who showed positive reaction to the Frei test and negative reactions to the Dmelcos, Ito and Wassermann tests. Only material which was proved to be culturally nonbacterial was employed. This material was injected intracerebrally into the monkeys and squirrels and subcutaneously, intraglandularly and intratesticularly into the guinea-pigs. The monkeys and the squirrels proved adapted to experimentation with the virus of the disease; emulsions of the brain and liver of these animals could be reinoculated into other monkeys or squirrels indiscriminately; the virus could be passed through as many as six squirrels and nine monkeys and could be used for testing the Frei reaction on other patients known to have lymphogranuloma inguinale. Even brain or liver of animals in which clinical symptoms (various pareses or paralyses of the extremities) failed to develop after inoculation furnished a potent antigen.

By means of these experiments the authors proved that the clinical entity known as inflammatory stricture of the rectum is a result of lymphogranuloma inguinale.

BRENNAN, Chicago.

CONGENITAL NONSYPHILITIC PEMPHIGUS: A REVIEW WITH THE DESCRIPTION OF A NEW DISEASE (EPIDERMOLYSIS BULLOSA HEREDITARIA LETALIS). G. HERLITZ, Acta pædiat. **17**:315, 1935.

In the differential diagnosis of bullous eruptions in the new-born infant congenital syphilis, the congenital form of pemphigus neonatorum contagiosus and epidermolysis bullosa hereditaria should be considered. Rarely, other possibilities must be considered, such as congenital variola or varicella, dermatitis herpetiformis and arsenical dermatitis. Examples of all these have been reported.

A review of the literature reveals the following facts concerning pemphigus neonatorum contagiosus: Although it is an infectious disease, it may be present at birth. The organism most commonly found in the lesions is the staphylococcus, although the streptococcus has been incriminated occasionally. The mode of infection is uncertain. The prognosis is usually good. The clinical features of both the simple and the dystrophic forms of epidermolysis bullosa hereditaria are too well known to require extensive description.

In the children's clinic of the university of Upsala, Sweden, within the last ten years eight cases of a peculiar congenital pemphigus have been encountered, the nosographic features of which are not identical with those of any of the foregoing entities. The disease is familial. The eight patients came from three families residing in different parts of the province of Upland, Sweden. All the patients were infants; both sexes were represented. At birth each patient exhibited either more or less widely distributed epidermal defects and bullous lesions or severe trophic disturbances of the nails of the fingers and toes. Usually all three types of lesions were present in the same patient. In six of the cases there was a slight tendency toward healing; in two cases atrophy of the bones and soft parts of the toes ensued. In two instances unidentified cocci were isolated from the bullae rather long after the latter had appeared. The patients usually remained afebrile. The disease was uniformly fatal within a few days or a few weeks after birth. Autopsy was performed in six cases but failed to provide significant information concerning the etiology or the pathogenesis of the condition. In one of the families the father and mother were cousins; in another the maternal grandparents were also cousins. Careful genealogic investigation of the families back to the beginning of the seventeenth century failed to unearth relevant data.

Although in these cases the condition presented several points of resemblance to epidermolysis bullosa hereditaria, it is justifiable to regard it as representing a separate entity because of the nature of the congenital epidermal defects, the atrophy of the skeleton, the fact that bullae could not be produced by means of friction and the uniformly fatal outcome. A total of fourteen cases of similar conditions have been described at different times and under different names since 1922 (Mautner, Kuse, Jenny, Heinrichsbauer). It is proposed to assemble these cases with those reported by Herlitz and to designate the condition as epidermolysis bullosa hereditaria letalis.

A copious bibliography is appended.

McCune, New York. [Am. J. Dis. Child.]

# Society Transactions

## SAN FRANCISCO DERMATOLOGICAL ASSOCIATION

JOHN M. GRAVES, M.D., *Secretary*

*Sept. 27, 1935*

L. R. TAUSSIG, M.D., *President*

LUPUS ERYTHEMATOSUS SHOWING FEATURES OF SARCOID, RESISTANT TO GOLD SODIUM THIOSULFATE BUT RESPONDING TO BISMUTH SUBSALICYLATE. Presented by DR. CHARLES ALBERT SHUMATE for DR. HARRY E. ALDERSON.

This patient was presented at the meeting of this society in December 1934 with the diagnosis of lupus erythematosus resistant to therapy with a gold, but responding to treatment with a bismuth preparation (ARCH. DERMAT. & SYPH. **32**:311 [Aug.] 1935). At that time there was discussion as to whether the disorder was syphilis, sarcoid or lupus erythematosus. Serologic tests were negative; the history was irrelevant; the results of biopsy suggested lupus erythematosus. The treatment had consisted of nine intravenous injections of 5 mg. of gold sodium thiosulfate at weekly intervals, and during the period of treatment the eruption on the face became steadily worse. Injections of gold sodium thiosulfate were discontinued, and eight injections of 2 cc. of bismuth subsalicylate were given. The patient improved until, at the time of the meeting, only slight involvement remained. Wassermann tests have been repeatedly negative, and biopsy by Dr. Ingels has revealed "lupus erythematosus showing features of sarcoid."

The patient was again presented before the society in March 1935 (ARCH. DERMAT & SYPH. **32**:987 [Dec.] 1935), after having received seven weekly injections of neoarsphenamine. The lesions had reappeared and extended over a more extensive area than when the patient was first seen.

Then nine intramuscular injections of 2 cc. of bismuth subsalicylate were given at weekly intervals. The face cleared entirely, and it has remained free from lesions. The lesions started to clear after the third injection. No local remedies were used.

EPIDERMOLYSIS BULLOSA. Presented by DR. MERLIN MAYNARD, San José, Calif.

This 5 month old baby is presented with a diagnosis of either epidermolysis bullosa or pachyonychia congenita. The history is as follows: Both the mother and grandmother have always had skins that blistered easily. For example, a wrinkle in a girdle caused a blister on the skin. Otherwise the family history is irrelevant.

At the time of birth blisters were noticed on the child's fingers. When the child was 3 days old these lesions were considered impetigo contagiosa and were treated as such. The baby was seen once by Dr. H. J. Templeton, who examined the lesions for thrush but found no fungi. The child was then in the St. Helena Sanitarium and Hospital, Sanitarium, Calif., for five weeks, where he was treated for impetigo. The baby has had thrush in the mouth throughout the disease. When I first saw the patient, on Aug. 23, 1935, definite lesions of impetigo contagiosa were present together with other lesions. The mother also had impetigo. However, I was surprised to find that the skin peeled to its full thickness and that bleeding occurred when a lesion was opened. As a result of treatment the impetigo has completely disappeared, but blisters containing clear fluid and not showing

evidence of inflammation continue to develop at all points of friction—such as the tips of the fingers, the elbows and the heels—after the application of adhesive tape, and from wrinkles in the bandages. Horny plugs, like small corns, have formed on the heels. No evidence of thrush has been found in the lesions. Nikolsky's sign is positive.

DISCUSSION

DR. MERLIN MAYNARD, San José, Calif.: I was much interested in an article on pachyonychia congenita by A. W. Sohrweide in this month's issue of the ARCHIVES (**32**:370 [Sept.] 1935). I have little doubt about the correctness of the diagnosis of epidermolysis bullosa, but I was interested in the fact that in this article it is stated that many features of this condition are also found in patients with pachyonychia congenita.

When the mother brought the child for examination she told me that the hands and feet sweated considerably. One finds the same thing in patients with pachyonychia congenita. The earliest occurrence reported was in a child aged 3 years. There has been no report of the occurrence of the disease in an infant.

I wonder whether pachyonychia congenita will develop in this child or whether pachyonychia congenita is a form of epidermolysis bullosa.

As far as treatment by the use of anterior pituitary is concerned, I wonder what might be a safe dose. I do not want to bring on precocious puberty, and I do not know what the effect in a child as young as this would be. I should appreciate suggestions as to diagnosis, treatment and dosage.

DR. H. J. TEMPLETON, Oakland, Calif.: To me this is the most interesting condition presented this evening, partly because I saw the patient several months ago for just one observation. At that time the baby had definite thrush of the mouth and pustular lesions of the body. Frankly, I did not think of a diagnosis of epidermolysis bullosa at that time. I was thinking instead of pyoderma or cutaneous thrush. I made cultures for thrush, but there was no growth. I have no experience with epidermolysis bullosa in infants and am not prepared to offer a diagnosis.

PARAPSORIASIS EN PLAQUES (BROCQ). Presented by DR. W. M. MEININGER for DR. A. E. INGELS.

J. E., a man aged 65, single, a native of Sweden, complains of a rash on the body, which has been present for over one year. He first noticed "spots" on the chest. They have caused no discomfort but have gradually spread over the trunk and upper extremities. There is no history of exposure to excessive heat. The patient had no previous similar eruption, and he makes no other complaints.

He had typhoid in childhood and suffered an injury to the skull, possibly a fracture, in 1912. He has had no venereal disease.

There are yellowish-brown, fairly well defined plaques about the size of a walnut on the trunk and upper extremities. Fine, adherent, almost imperceptible scales are present. The lesions are not infiltrated. There is an erythrosquamous eruption on the dorsa of both hands. Dentition is poor; there are many crowned and some devitalized teeth. Other results of physical examination were essentially negative.

The Wassermann reaction of the blood was negative. The blood count gave normal results. A biopsy was made. Dr. Ingels will present sections.

The diagnosis is parapsoriasis en plaques (Brocq).

DISCUSSION

DR. W. M. MEININGER: We have not treated the patient, but apparently he has used some remedies which are responsible for the erythematous areas. I think that the duration of the lesions, their character and the lack of infiltration and of subjective sensation justify a clinical diagnosis of parapsoriasis.

DR. A. E. INGELS: The sections show a mild nonspecific round cell infiltration. There is nothing characteristic so far, although it seems that one can exclude some possibilities which have to be considered in this case. The absence of plasma cells excludes syphilis. The absence of migration of leukocytes and the absence of micro-abscesses seem to exclude psoriasis. The appearance of the sections excludes simple neurodermatitis and pityriasis rosea.

Because I wondered about the correctness of the diagnosis I should like to throw some doubt on the results of treatment of parapsoriasis. Dr. Chipman has reported the cure of parapsoriasis by local applications, and I understand that some dermatologists believe that anthralin (di-hydroxyanthranol) effects a cure. Was the diagnosis correct in the cases which Dr. Chipman reported, and is it beyond doubt in this case?

DR. G. V. KULCHAR: To me the diagnosis of parapsoriasis has always been a clinical, not a histologic one. Parapsoriasis is a dermatosis in which there occur plaques which are yellowish in the center, as described by Crocker. At least this dermatosis fits into no other classification, and for that reason it has been classified as parapsoriasis.

DR. H. J. TEMPLETON, Oakland, Calif.: It is important to differentiate this condition from the preinfiltrative stage of mycosis fungoides.

DR. HARRY E. ALDERSON: My co-workers and I have seen this man a number of times, and there was no evidence of itching. He also stated that there was no itching. We have considered the diagnosis of a prefungoid condition, and the disorder may develop into a frank granuloma fungoides, as some of the eruptions diagnosed as parapsoriasis do.

LYMPHOGRANULOMA INGUINALE. Presented by DR. N. N. EPSTEIN.

P. C., a man aged 38, a Lithuanian, a cigar clerk, entered the University of California Hospital on Sept. 2, 1935, and was discharged on Sept. 27, 1935.

Nine days before admission to the hospital the patient noticed a small abrasion on the dorsal surface of the sulcus. He began to have chills and fever four days later, and simultaneous enlargement of the right inguinal lymph nodes was noted. There is a history of sexual intercourse with a Negress six and twelve weeks before the appearance of the sore.

The patient had a primary sore in 1925, after the appearance of which he received four or five intravenous injections. He has received no treatment since.

A dime-sized ulcer is present on the sulcus, and there is a large tender mass in the right groin. The temperature was 38.2 C. (100.76 F.). Dark-field examination failed to show Spirochaeta pallida. Four more dark-field examinations made while the patient was in the hospital also gave negative results. The Wassermann and the Kahn reactions of the blood were negative on Sept. 19, 1935.

The Frei test gave a 4 plus reaction. About 100 cc. of pus was aspirated on two occasions. Examination of the blood on Sept. 2, 1935, showed 10,250 white cells and 79 per cent polymorphonuclears; on September 5 there were 16,300 white cells and 84 per cent polymorphonuclears.

Treatment has consisted of rest and application of an ice-bag.

The diagnosis is lymphogranuloma inguinale.

DISCUSSION

DR. N. N. EPSTEIN: This patient presents an excellent example of lymphogranuloma inguinale, and the fact that the primary lesion was present furnished an opportunity to study it from the beginning.

The amount of fever present was striking. The temperature became normal when free drainage was established. It is unusual that the primary lesion should persist for this length of time.

I wish to ask Dr. Levin how accurate he thinks the Frei test is.

DR. E. A. LEVIN: Those who have done much work with the disease believe that the test is specific. However, in early stages of the infection it is possible for the Frei test to be negative. In a study of thousands of cases it has been found to be negative in cases of venereal diseases other than lymphogranuloma inguinale. The test apparently may remain positive throughout the patient's life. The longest period reported for a positive test was thirty-nine years; that occurred in a patient with a residual scar.

DR. F. G. NOVY JR., Oakland, Calif.: We secured 100 cc. of pure pus in this case, which we tried to culture for the filtrable virus, and so far the results of the cultures have been negative.

MULTIPLE HEMORRHAGIC FAMILIAL TELANGIECTASIA OF THE SKIN AND MUCOUS MEMBRANE (OSLER). Presented by DR. H. J. TEMPLETON, Oakland, Calif.

H. D. S., aged 23, was first seen at the E. V. Cowell Memorial Hospital, Berkeley, Calif., about Sept. 1, 1935, being referred by Dr. Howell of Berkeley. The patient complained of nosebleeds and of pinhead-sized red spots on the lips and face.

There are many pinhead-sized telangiectatic spots on the cheeks, on the lips and on the nasal mucosa. The patient states that his father and brother suffered from the same disorder. A diagnosis of multiple hemorrhagic familial telangiectasia of the skin and mucous membrane was made. Treatment has consisted of destruction by means of electrodesiccation or the actual cautery.

DISCUSSION

DR. H. J. TEMPLETON, Oakland, Calif.: This is apparently a clearcut case of Osler's multiple hemorrhagic familial telangiectasia of the skin. The patient's father and brother had the same disorder.

I have wondered as to whether or not any such treatment as that which has been used for hemophilia, that is, injection of ovarian substance or of snake venom might be of value in this case.

A CASE FOR DIAGNOSIS (IODODERMA?). Presented by DR. H. J. TEMPLETON, Oakland, Calif.

Mr. S. J. D., aged about 65, presented himself on Aug. 19, 1935, because of many papulopustular necrotic lesions on the trunk. The lesions vary from small red papules 3 mm. in diameter to pustular and necrotic areas from 3 to 5 mm. in diameter and to acneform cystic lesions about 1 cm. in diameter. As the necrotic lesions heal, some scarring remains.

The patient had been taking potassium iodide before the onset of the eruption. The Kline test was negative. A differential blood count showed 11,525 white cells, 70 per cent polymorphonuclears, 26 per cent small lymphocytes, 1 per cent large lymphocytes and 3 per cent eosinophils. An intradermal test with tuberculin was strongly positive.

In making the diagnosis, iododerma and papulonecrotic tuberculid were considered. Daily intravenous injections of a 2 per cent solution of sodium chloride have produced only a moderate degree of improvement in a month. The section which is presented shows a picture compatible with papulonecrotic tuberculids.

DISCUSSION

DR. G. V. KULCHAR: I think that iododerma is well ruled out. There are no lesions over the face. The character of the lesions suggests acne scrofulosorum or tuberculid.

DR. HARRY E. ALDERSON: I think that a diagnosis of some form of tuberculosis can be established. Has auto-inoculation been tried?

DR. A. E. INGELS: I wish I had seen some other sections stained for acid-fast bacilli and elastic and connective tissue. I did not see any foci of caseation; the absence of such foci would be absolutely against a diagnosis of papulonecrotic tuberculid. The absence of acanthosis practically excludes an iododerma.

DR. F. G. NOVY JR., Oakland, Calif.: I did not feel that the disorder was an iododerma or a papulonecrotic tuberculid. The pustules are clearing much faster than papulonecrotic tuberculids ordinarily do.

DR. MERLIN MAYNARD, San José, Calif.: I considered the condition to be acne cachecticorum or acne conglobata. The tuberculids are often more solid than this lesion.

URTICARIA PIGMENTOSA IN AN ADULT. Presented by DR. HARRY E. ALDERSON.

Mr. F. W. G., a man aged 35, a carpenter, entered the dermatologic clinic of the Stanford University Hospitals on Sept. 10, 1935, because of cutaneous trouble which had lasted for "several" years. He stated that when he became overheated or when he rubbed the lesions they swelled up, popped up. Otherwise no discomfort from the lesions was ever experienced. He could not tell whether the lesions vanished completely, to recur as new ones in other locations.

A general examination was made by one of the physicians on the medical service, and no abnormalities, except an anal fistula, were found.

The personal and the family history are irrelevant.

The Wassermann reaction of the blood was negative on September 13.

There is a generalized eruption of a maculopapular-nodular character over the trunk and extremities. The face, palms and soles are not involved. The lesions are ill defined, brownish and discolored; only a few show a more vivid reddish color. When rubbed, a number of them become urticarial and raised above the surface of the skin.

A biopsy was made on September 12. Sections (stained by the hematoxylin-eosin, silver nitrate, elastin H. and Van Gieson methods) are presented for examination.

DISCUSSION

DR. HARRY E. ALDERSON: In cases of these disorders the question occasionally arises whether or not the condition is urticaria pigmentosa or urticaria with pigmentation. No mast cells were seen, it is true, but it is known that sometimes they are not found, and a later biopsy may show the typical picture.

DR. A. E. INGELS: I should like to challenge opinion as to this condition, particularly in this case. In the sections there are practically no mast cells. The outstanding feature is the deep pigmentation of the basal cell layer and prickle cell layer. I should like to hear the members' opinion regarding the sections.

DR. MERLIN MAYNARD, San José, Calif.: I looked at the sections. It is true, of course, that there are many cases in which the clinical picture is that of urticaria pigmentosa and in which sections do not show mast cells. The pathologic picture is lacking in the one characteristic which establishes a diagnosis of urticaria pigmentosa.

A CASE FOR DIAGNOSIS. Presented by DR. H. V. ALLINGTON for DR. C. J. LUNSFORD, Oakland, Calif.

Mrs. M. was first seen on September 19 because of hypertrophy and tenderness of the soft tissue overlying the hard palate in the area covered by a partial plate which she has worn for the last ten years. The affected tissue is thrown into deep rugae, with individual islands of tissue resembling lymphangiomatous tissue.

The condition was first noted, from three to four months ago, because of the discomfort which it caused, and the patient has been somewhat more comfortable since her plate was adjusted by her dentist. The condition has improved somewhat since the plate was removed entirely.

DISCUSSION

DR. H. V. ALLINGTON: My co-workers and I believe that the disorder represents a reaction to irritation from a plate. In a conversation with a dentist about this condition I was told that he had seen it in several patients. He suggested as treatment the accurate fitting of plates and the wearing of metal rather than of rubber plates. He expressed the opinion that rubber may cause degeneration and sluggishness of the tissues because, being a poor caloric conductor, it deprives the tissues of the stimulating effects of heat and cold.

DR. L. R. TAUSSIG: Has any attempt been made to find out whether the patient is sensitive to hard rubber?

DR. H. V. ALLINGTON: A patch test was made, and no sensitivity was found. Temporary relief followed the removal of the plate.

RADIATING TELANGIECTASIA OF THE LOWER PORTION OF THE LEGS. Presented by DR. C. J. LUNSFORD, Oakland, Calif.

This woman, aged about 25, presents on the extensor surfaces of the lower portions of both legs and on the ankles, running down onto the dorsa of the feet, superficial spreading small blood vessels, which form a network. In some places there appears to be a central blood vessel from which the small branches extend. Altogether the appearance is that of a large spider nevus.

The patient states that the telangiectasia has been present for years. She states that it is not present in the morning when she awakens but that it immediately appears when she steps on her feet.

There are no subjective symptoms. Aside from some enlarged varicose veins, no abnormalities are known to be present.

RADIATING TELANGIECTASIA OF THE LEGS. Presented by DR. H. V. ALLINGTON.

Miss C., a Portuguese woman aged 38, is presented with a diagnosis of radiating telangiectasia of the legs. The patient has a diffuse telangiectatic network over the lower third of each leg and ankle, which began about ten years ago and has slowly become more extensive.

The patient had measles and mumps in childhood. She often suffered from sore throat before she underwent a tonsillectomy at the age of 25. Since 1928 she has had frequent spells of tachycardia, fatigability and mild precordial pain. Careful studies of the heart have failed to reveal any chronic abnormalities, although there is a slight right axis deviation in the electrocardiogram, and a periodic slight cyanosis has suggested the presence of some mild congenital cardiac anomaly, such as a partially patent foramen ovale or ductus arteriosus. There is mild swelling of the ankles during hot weather. The patient also suffered from pain in the right lower quadrant of the abdomen for several years; after a laparotomy was performed a year ago, at which time a chocolate cyst over the right ovary was removed, the pain disappeared.

Extensive laboratory work has given negative results. The patient has felt somewhat better since she took thyroid, although in 1928 her basal metabolic rate was reported as + 14 per cent.

DISCUSSION

DR. H. J. TEMPLETON: In the past ten years my co-workers and I have observed six or eight cases of this condition, which fits in, I believe, with what is described by Edel as radiating telangiectasia of the legs (*Brit. J. Dermat.* **38**:112 [March] 1926).

DR. ORLAND F. MONTGOMERY: In the cases I have observed the lines have converged into the ankle.

DR. G. V. KULCHAR: I disagree with the diagnosis as presented. The radiating type of telangiectasia with which I am acquainted is more like a spider nevus, radiating in various directions. These lesions, to my mind, conform to the syndrome

described by Parkes Weber. Such lesions are usually due to exposure to the elements. I think he called the disorder erythrocyanosis puellorum.

DR. H. V. ALLINGTON: One of the two patients had a thorough examination. It is believed that there is some possibility of a congenital cardiac lesion in this patient, although it has been impossible to prove the existence of such a lesion.

DR. HARRY E. ALDERSON: A young woman whom I saw on a hike in the high mountains jumped into a pool of ice-water in the evening after a long climb. Telangiectasia of this character promptly followed.

A CASE FOR DIAGNOSIS. Presented by DR. ORLAND F. MONTGOMERY.

A. Y., a woman aged 23, single, a Japanese, states that except for a scaly scalp she had always been well until March of this year, when a weeping eruption developed about the ears and nostrils. Within a week an almost complete alopecia resulted. There is no history of fever. The eruption later extended to the pubic region, axillae and thighs. Menstruation, which was formerly normal, has been completely suppressed save for a normal period early in August. The patient complains that her skin has always been dry.

When the patient was seen first, in July, there were (1) general ichthyosis, which was mild, (2) almost complete universal alopecia, (3) moist and vegetating massive dermatitis, noteworthy because of its complete symmetry, about the ears, nose, axillae, pubic region, inner and dorsal aspects of the thighs and dorsal aspects of both feet.

The impression was that the patient was suffering from a debilitating and wasting disease.

Laboratory examinations revealed nothing noteworthy save a hemoglobin content of 70 per cent, a corresponding reduction in red cells and a color index of 1. There were changes in the size and shape of the red cells suggesting a primary anemia. The basal metabolic rate was not determined.

DISCUSSION

DR. ORLAND F. MONTGOMERY: This patient is presented for diagnosis and therapeutic suggestions. I cannot find a diagnosis that fits the disorder. Under treatment the eruption was clearing up, but it recurred. The eruption was above the umbilicus at one time. The eruption below the waist cleared up almost entirely and then recurred. When it was first seen it was tremendously vegetating, the lesions having almost a cauliflower-like appearance. From the appearance of the lesion around the scalp some one suggested the diagnosis of psoriasis. No fungi have been found.

I think that this patient is definitely ill and has been ever since I have seen her. She has had some form of avitaminosis. Because of the complete symmetry of the eruption I am inclined to believe that it is constitutional. I should be surprised to see a seborrheic lesion as symmetrical as that. I spoke to a neurologist about the case, and he thought that the disorder might be a trophic disturbance.

DR. HARRY E. ALDERSON: Have experiments with auto-inoculation been tried?

DR. ORLAND F. MONTGOMERY: No such experiments have been made.

DR. HARRY E. ALDERSON: The well defined character of the main process and the sharply defined outlying islands suggested to me, as they did to Dr. Montgomery in the beginning, that the disorder might be a mycotic process. I suppose the patient has tried a great deal of home therapy?

DR. ORLAND F. MONTGOMERY: No, I do not think she has. As to food, she has had an average diet. It is known that the Japanese are much inclined to have eczema.

DR. H. V. ALLINGTON: The lesions look like those reported by Hopkins to be due to infection with a yeast. In his cases, I believe, he considered the possibility that an intestinal infection due to a yeast was responsible for the symptoms.

Dr. Merlin Maynard, San José, Calif.: I have observed two cases of disorders similar to this. Both occurred in young Italian girls shortly after puberty. In both girls the disorder began with lesions behind the ears; these were followed by a generalized eczematoid dermatitis such as is presented by this patient. I got nowhere as far as treatment was concerned in either of these cases, except for bringing about temporary relief, as Dr. Montgomery has done.

My opinion is that the disorder is probably a sensitivity of the skin to staphylococci. I think also that the theory that an avitaminosis is responsible is a good one. To one girl I gave viosterol, but it did no good. To the other I gave iron and ammonium citrates, and that did no good either. The girls were both chloremic. In one the hemoglobin content of the blood was 55 per cent.

Dr. G. V. Kulchar: The distribution, the well defined border and the character of the lesion, in addition to the prostration—the whole picture—make the diagnosis of pellagra certain.

Favus. Presented by Dr. N. N. Epstein.

S. Z., a woman aged 21, was born in Illinois but has lived in Modesto, Calif., since early childhood. Her condition dates back about ten years, when a slowly progressive loss of hair with scaling and crusting was noticed about the scalp. A change in several nails of each hand occurred, causing discoloration and brittleness of the involved nails.

The patient was first seen in March 1930, when scarring and scutula were present in numerous areas throughout the scalp. These have gradually extended. The involvement of the finger-nails has progressed slowly.

Microscopic examination of involved hairs showed mycelial threads along their long axis. Culture confirmed the diagnosis of infection with Achorion Schoenleinii.

DISCUSSION

Dr. N. N. Epstein: This patient has been under my observation for four years. The condition has progressed slowly, gradually involving a large part of the scalp. The inflammation about the hair follicles is slight, considering the amount of fungus found in the lesion.

The patient has lived in Modesto, Calif., and is a white girl. She has not been under constant observation for longer than a couple of weeks at a time. I should like to know the members' opinion as to prognosis at the present time.

Dr. Stuart C. Way: Several months ago I discussed this case with Dr. Epstein and suggested that the lesions, a few at a time, be lightly treated with phenol and that the following formula be applied once daily to the entire scalp: thymol, 2 Gm.; iodine crystals, 1.2 Gm.; turpentine, 20 cc.; olive oil in quantity sufficient to make 60 cc.

Lupus Erythematosus Resistant to Intravenous Administration of a Gold Preparation But Responding to Intramuscular Administration of a Bismuth Preparation and to a Vegetable Diet. Presented by Dr. A. E. Ingels.

Mr. H. H., aged 50, a janitor at the Laguna Honda Home Infirmary, has been treated at the outpatient clinic of that institution since November 1933. His lupus erythematosus had lasted from twelve to fifteen years, according to the note on his treatment sheet. Presumably his disorder involved the entire face, the ears and some parts of the scalp.

This patient was seen first as an outpatient and has been observed for two years. Dr. Epstein has seen him intermittently, and he and I have seen the patient for approximately one year each. He has received in all fifty-eight injections of a gold preparation, with strikingly little effect. He would improve for a short while, but the condition would recur.

I finally thought that bismuth should be tried, and I also ordered a vegetable fat diet. The patient has received six weekly injections so far, and marked improvement started within fourteen days.

DISCUSSION

DR. N. N. EPSTEIN: When I first saw this patient he had extensive lupus erythematosus; and I believed that treatment with a gold preparation had resulted in about 50 per cent improvement. The condition remained stationary between courses of treatment with the gold preparation. Certainly his appearance tonight is entirely different from that which he presented when I last saw him. The lesions are much more superficial than in most cases of lupus erythematosus. I agree with Dr. Ingels that in this case bismuth certainly has done a great deal for the patient.

DR. H. J. TEMPLETON, Oakland, Calif.: I should like to make one remark about the dosage of gold and sodium thiosulfate. Physicians have been rather cautious of late about dosage and have not administered more than 100 mg. Recently, however, my co-workers and I treated a patient with discoid lesions of the face in whom conservative doses produced no benefit. Increasing the dose to 250 mg. per week has caused all of the lesions to disappear. He is the only patient to whom we have given such large doses.

DR. STUART C. WAY: The use of preparations containing bismuth is not new in the treatment of lupus erythematosus. An excessive amount of fibrosis, however, renders it less efficient.

DR. A. E. INGELS: I was much interested in Dr. Templeton's remark about dosage. Expert dermatologists in Germany have expressed almost unanimously, in a résumé of the subject, the opinion that the dose should be as low as possible. That reminds me of a patient to whom 100 mg. was given by mistake, causing an almost fatal flare-up of the disease.

DR. L. R. TAUSSIG: It was interesting this summer to hear a paper on the subject by Wright, who is associated with Schamberg's clinic. He has used doses from 100 mg. up as a routine. It was interesting, however, in going over a considerable series of his cases to find that he had two fatalities which could be traced to the toxic effect of the gold preparation and that at least 25 per cent of the patients showed toxic symptoms. I think that that report alone would make one hesitate to resort to large doses. In the French literature there are many reports of toxic eruptions due to gold preparations, evil results being apparently more frequent than with neoarsphenamine. That, I believe, is due to the fact that French physicians have used doses much higher than those administered in this country.

DR. STUART C. WAY: In 1922, when I used gold in the form of krysolgan, the doses were usually larger, and the reactions were severe indeed.

KERATOSIS PILARIS. Presented by DR. N. N. EPSTEIN.

M. M., a man aged 24, was first seen in August 1933, at which time he complained of an extensive erythematofollicular eruption over the trunk and arms. The lesions consisted of accuminate papules situated about the hair follicles. There were no associated symptoms. The condition has remained the same during the past two years; altogether it has been present about four or five years.

DISCUSSION

DR. N. N. EPSTEIN: This patient is presented simply because of the extent of the condition.

DR. ORLAND F. MONTGOMERY: I disagree with the diagnosis. The arms and legs are quite free from eruption. The distribution plus the degree of inflammatory reaction leads me to believe that the disorder is not keratosis pilaris.

DR. H. J. TEMPLETON, Oakland, Calif.: I think that this is the type of keratosis pilaris which the French call keratosis pilaris rubra.

DR. A. E. INGELS: I wish to call attention to the appearance of epithelioma adenoides cysticum, which may take on a similar appearance, including the presence of lesions on the fingers. One might keep that in mind as a possibility.

LYMPHANGIOMA OF THE TONGUE. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

Mr. Z., aged 21, was first seen by me at the E. V. Cowell Memorial Hospital, Berkeley, Calif., on about Sept. 1, 1935, because of extreme swelling of the anterior third of the tongue.

Inspection revealed a lymphangioma measuring about 1½ inches (3.8 cm.) in diameter. The patient stated that this had been present since he was 6 years old but that it had never been treated because of religious reasons. At varying intervals it swells to huge proportions, interfering with speech and the ingestion of food. The patient is presented for suggestions as to therapy.

DISCUSSION

DR. H. J. TEMPLETON, Oakland, Calif.: I should like to have opinions as to the wisdom of implanting radium seeds in this mass.

DR. L. R. TAUSSIG: Radium is not very effective in the treatment of lymphangioma. I should hesitate to implant radon seeds in this patient's lesion. I believe that even though it is extensive, the lesion could be desiccated; treatment should be applied to a small portion at a time, gradually extending over the whole area, the work being done from the edges toward the center.

DR. STUART C. WAY: I wonder whether the actual cautery would not be more efficient than electrodesiccation.

COCCIDIOIDAL GRANULOMA. Presented by DR. FRANCIS TORREY.

E. C., a Negro girl aged 11 years, was first seen on July 1, 1935, at the San Francisco Hospital. At that time she had had pain in her right hip for three months and complained of increasing difficulty in walking and of a "lump" in her back which had been present for two months.

She lived in Texas until she was 3 years old, in San Francisco till the age of 6 years, in Bakersfield and Tulare (San Joaquin Valley) Calif., from the age of 6 to that of 7½ years and in San Francisco from 7½ to 11 years.

Four years ago, while she was living in Tulare County, the child first complained of pain in the region of the lower right ribs; this continued up to her admission to the hospital in July 1935. An abscess developed on the back while the child was in the hospital. Cultures made from aspirated material were positive for Coccidioides.

Roentgenograms revealed destruction of the right ilium and sacro-iliac joint. The fourth, fifth, sixth, seventh and ninth vertebrae showed extensive destruction posteriorly and a paravertebral abscess. Cutaneous tests for coccidioides were negative.

The history was irrelevant, and physical examination disclosed no abnormalities except a fluctuant, nontender mass the size of a small orange located posteriorly at the level of the eighth to the tenth thoracic vertebra. The temperature has been normal since the child left the hospital.

Treatment has consisted of injections of 5 cc. of a 1 per cent solution of antimony and potassium tartrate twice a week (eighteen injections have been given), rest in bed, a regular diet and administration of cod liver oil and a mixture of 4 cc. of iron and copper three times a day.

DISCUSSION

DR. FRANCIS TORREY: This child lived in the San Joaquin Valley for one and a half years. She has been in San Francisco for three and a half years. Four years ago she complained of pain in the region of the lower right ribs which continued until she entered the hospital in July 1935. In April 1935 she could not walk because of severe pain in the right hip. Roentgenograms showed involvement of the pelvis and of one rib.

DR. N. N. EPSTEIN: I think it is interesting that roentgenograms were the first means of examination that led to a diagnosis.

DR. L. R. TAUSSIG: What were the roentgenologic characteristics of the involvement?

DR. N. N. EPSTEIN: I could not say exactly. The appearance was similar to that of tuberculosis but not exactly like it.

DR. C. E. SCHOFF, Sacramento, Calif.: Dr. Jacobsen reported a case which occurred in Los Angeles in which there was a primary pelvic involvement. It would be interesting if it could be determined whether this patient's infection was primarily in the pelvis.

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## PITTSBURGH DERMATOLOGICAL SOCIETY

JOSEPH J. HECHT, M.D., *Secretary*

*Sept. 19, 1935*

EMERSON GILLESPIE, M.D., *President*

MONILIASIS. Presented by DR. STANLEY CRAWFORD.

C. P., a Negro boy aged 10 years, has a marked involvement of the lingual and buccal mucosa with whitish patches producing a downlike appearance due to infection with Monilia. The first and second finger-nails of the right hand are thickened, dystrophic and dirty brownish, and the two fingers show a padlike paronychia. Cultures made by Dr. Moore, of St. Louis, revealed Saccharomyces albicans.

The child has received iodides. On one occasion a bullous erythema multiforme developed. At present there are rounded, dusky red purpuric macular lesions due to the iodide on the arms, legs and trunk. The vertex of the scalp is entirely covered with amber crusts. Crusting is also present over the bridge of the nose and in the angles of the mouth, and there is an acute purulent conjunctivitis.

DISCUSSION

DR. C. B. NORRIS, Youngstown, Ohio: I should like to know if the diagnosis was reached before the culture was made and how the nails became infected?

DR. F. M. AMSHEL: At first glance the lesions on the legs appeared to have the color typical of an eruption due to phenolphthalein, and I thought that the disorder was caused by that drug. The remains of the bullous lesions on the hands can be seen, and these together with the history of ingestion of iodides make it probable that the condition is an eruption due to iodide.

DR. STANLEY CRAWFORD: In answer to Dr. Norris' questions I wish to state that the tongue showed typical whitish patches. The neighboring mucosa also showed the whitish patches. The fingers involved were the thumb and the next finger of the right hand, the two fingers which the child would most likely put in his mouth. There was also a red paronychia of these fingers. This was quite stubborn and failed to respond to many treatments which were tried. I shall try application of gentian violet and shall report at a future meeting as to results.

Monilia also attacks the lungs, causing fibrosis and perhaps asthenia and death. If this is treated early with iodides the prognosis is better.

A CASE FOR DIAGNOSIS. Presented by DR. M. W. RUBENSTEIN.

J. S., a girl aged 6½ years, about five weeks ago complained of pain in the abdomen. A local physician gave her a liquid diet. The physical examination at that time apparently gave negative results. The patient's appetite remained good. She was then put on a limited liquid diet and was given medication by mouth. About three weeks ago an eruption appeared on the abdomen and back. Within a few days it spread to the palms and soles, consisting at that time of pruritic papules. Within the past few days bullous lesions have appeared on the palms and soles. The pain in the abdomen lasted for about two weeks. During the first two weeks of illness the temperature fluctuated between 99 and 100 F. Lately the child has complained of soreness of the finger-tips.

DISCUSSION

DR. B. A. GOLDMANN: I believe the disorder is toxic erythema which possibly began as an acute dermatophytosis of the palms and soles.

DR. STANLEY CRAWFORD: I think that this is a case of acrodynia. This diagnosis is suggested by the characteristic flaccid posture of the child, the so-called "pretzel position." I admit that not all the classic signs, such as pain, fretfulness, etc., are present, but the mother stated that the child had complained of severe itching of the palms and soles. It may be too early for these classic signs to be present, or they may not appear at all.

DR. M. W. RUBENSTEIN: I saw this patient for the first time this afternoon. I cannot consider the diagnosis of acrodynia. A child with acrodynia is fretful, cries and whines all the time, does not want to eat, is cold and clammy and has painful hands. The patient does not show these signs.

NOTE.—The patient was sent to the hospital and was apparently getting well. After she had been in the hospital for three weeks she died suddenly; there was no apparent cause of death. Permission for autopsy was not obtained.

A CASE FOR DIAGNOSIS (MYELOID LEUKEMIA?). Presented by DR. H. T. PHILLIPS, Wheeling, W. Va., and J. C. KERR, McKeesport, Pa.

Mr. G. E., aged 38, complains of a papulonodular eruption of several years' duration. The color is from normal to reddish brown, and the involvement is symmetrical and generalized. Periods of regression and of exacerbation have occurred, and occasionally itching has been intolerable; at other times there have been no subjective symptoms.

The patient was in a sanatorium in 1929 for pulmonary tuberculosis; during his sojourn there roentgenograms showed tuberculous involvement, but examination of the sputum never gave positive results. Cutaneous lesions appeared first while the patient was in the sanatorium. The Wassermann and the Kahn test were negative. A blood cell count on Aug. 23, 1935, showed 3,610,000 red cells, 57 per cent hemoglobin and 12,450 white cells. The results of the differential count were as follows: polymorphonuclears, 66 per cent; small lymphocytes, 26 per cent; large lymphocytes, 7 per cent; eosinophils, 1 per cent. Biopsy showed a picture resembling that of myeloid leukemia.

Another blood count, on Sept. 17, 1935, showed 75 per cent hemoglobin, 3,760,000 red cells and 9,500 white cells. The results of the differential count were as follows: polymorphonuclears, 60 per cent; small lymphocytes, 26 per cent; large lymphocytes, 7 per cent; eosinophils, 2 per cent; transitionals, 2 per cent; large monocytes, 3 per cent.

The patient has received four roentgen treatments of one-half erythema dose to the anterior aspect of the right thigh; smoothing of the lesions and disappearance of the itching have resulted.

DISCUSSION

DR. F. M. AMSHEL: I thought, at first glance, that I saw flat, shiny angular papules resembling lichen planus or even a vesicular lichen planus, but of course the fact that the lesions are nodular made me change my mind.

DR. B. A. GOLDMANN: Have any abnormal cells been seen in the smears? I wish Dr. Phillips would send me a smear. A polychrome stain would show the different cells.

DR. F. M. JACOB: Immature cells respond to roentgen radiation, and since in this case the disorder has responded to radiation some immature cells must have been present.

DR. J. C. KERR, McKeesport, Pa.: When we first saw this patient we thought he had leprosy. The leonine expression due to the nodular involvement of the ears and face was present, but this occurs also in patients with leukaemia cutis.

EPIDERMOLYSIS BULLOSA. Presented by DR. STANLEY CRAWFORD.

K. M., a Negro girl aged 12, has had a marked reticulated atrophy over the anterior and posterior aspects of the trunk, buttocks and upper and lower extremities and over the neck and face for the past five years. The skin feels dry and shows numerous small rounded scars from bullae which appeared spontaneously. There is atrophy of the skin of the body and face. The anterior surface of the neck shows numerous scars of bullae. The dorsal surface of both hands and of all the fingers is atrophic and shows flaccid bullae which develop after the slightest trauma. The tongue is atrophic and shows rounded reddish areas along the sides and anterior portion of the dorsal surface. The skin of the eyelids is atrophied, but there is no ectropion.

DISCUSSION

DR. B. A. GOLDMANN: I believe that this is a case of congenital ichthyosiform erythroderma.

DR. F. M. AMSHEL: I agree with Dr. Goldmann.

DR. F. M. JACOB: Dr. Beinhauer has used theelin in two cases with success. The patients were a male and a female.

DR. STANLEY CRAWFORD: There is no ichthyosis in this case. There may appear to be on sight, but when the hand is run over the skin it is found to be smooth. The skin is atrophic, and this atrophy throws the skin into lozenge-shaped markings. Few of the nails are shed. I shall try Dr. Jacob's suggestion on therapy and shall report the results at a future meeting.

ERYSIPELOID. Presented by DR. H. T. PHILLIPS, Wheeling, W. Va., and DR. J. C. KERR, McKeesport, Pa.

Mr. E. R., aged 25, a butcher, presented purplish-red, flat, smooth lesions with slightly elevated edges over the dorsum of the left thumb and hand; the lesions are of ten days' duration. The patient states that he scratched the back of the thumb while cleaning poultry three days before the eruption appeared. There is slight itching, but no constitutional symptoms are present.

DISCUSSION

DR. H. T. PHILLIPS, Wheeling, W. Va.: I spent my vacation last summer at a resort where crabs are plentiful. I asked a fisherman whether they get bitten often. He said that they did and that occasionally blood poisoning, which is evidently an erysipeloid, resulted. The crabs perhaps get hold of some stale meat. The fisherman said that he applied poultices to the arm and that in two weeks the disorder generally got better. I believe that if nothing is done the eruption will heal.

ERYTHEMA NODOSUM WITH LESIONS ON THE FACE. Presented by DR. H. T. PHILLIPS, Wheeling, W. Va., and DR. J. C. KERR, McKeesport, Pa.

Mrs. R. F., aged 36, presents nodular, pink to bluish lesions on the anterior and lateral surfaces of each leg. In addition, she has indurated lesions over the forehead, nose and cheeks. The eruption has been present for two weeks. There is no history of previous illness, but the patient has complained of slight pain in the wrist and elbows since the eruption began.

DISCUSSION

DR. H. T. PHILLIPS, Wheeling, W. Va.: I did not know what to call the condition on the face, but probably it should be considered a part of the general condition.

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JOSEPH J. HECHT, M.D., *Secretary*

*Oct. 17, 1935*

EMERSON GILLESPIE, M.D., *President*

A CASE FOR DIAGNOSIS (LEPROSY?). Presented by DR. M. W. RUBENSTEIN and DR. M. PETTLER, Beaver Falls, Pa.

W. H., a married man aged 60, was seen by Dr. Rubenstein on May 28, 1935, at which time he presented lesions that resembled a dermatitis due to phenolphthalein or possibly mycosis fungoides. At that time he also presented atrophy of the muscles of the thenar eminence of the left hand and of the left interossei muscles. Both ulnar nerves were enlarged. The patches of dermatitis were hyperesthetic rather than anesthetic.

Dr. J. A. Mitchell stated that the illness began in June 1934. At the onset there were severe chills, high fever and profuse sweating. The history revealed that the patient had malaria while he was in the Spanish-American War in the Philippines. Physical examination in August 1934 gave the following results: The heart beat was irregular; the temperature was 100 F.; the pulse rate was 88; the abdomen was distended; the liver, kidneys and spleen were not palpable; there were intense cyanosis of all the fingers and toes, of the lobes of the ears and of the tip of the nose and edema of several fingers and toes approaching a wet type of gangrene. In addition, there were purpuric spots on the arms and legs varying in size from that of a 5 cent to that of a 50 cent piece. The patient was semicomatose. He was treated at that time by administration of digitalis and thyroid, forcing of fluids and injections of dextrose. Within a few days the cyanosis improved with exception of that of four toes of the left foot, three toes of the right foot and two fingers of the left hand. In these the process progressed to a dry gangrene and loss of the terminal phalanges. There was very little pain. In February 1935 a macular eruption associated with a marked stinging and burning sensation developed over the entire body, especially over the back. The patient stated that he had taken phenolphthalein occasionally. Ingestion of phenolphthalein was discontinued, and the lesions progressed to an indurated stage.

Examination of the blood on Nov. 4, 1934, showed 4,400,000 red cells and 8,900 white cells. The results of the differential count were as follows: polymorphonuclears, 71 per cent; lymphocytes, 20 per cent; monocytes, 4 per cent. The Wassermann and the Kahn test and cutaneous tests with quinine salts were negative. Examination of fresh blood for parasites gave negative results. Examination of the urine showed a 2 plus reaction for albumin and a negative reaction for sugar. The specific gravity was 1.015; there were no casts.

Biopsy of two specimens was reported to show chronic granulomatous infiltration.

DISCUSSION

DR. G. J. BUSMAN: The diagnosis is consistent with the clinical picture. However, a diagnosis of leprosy should not be made unless the Hansen bacillus has been demonstrated.

DR. H. T. PHILLIPS, Wheeling, W. Va.: I am not willing to accept the diagnosis, although the symptoms, such as loss of eyebrows, hyperesthesia and atrophy of the interossei muscles are indicative of leprosy. The organism has not been recovered although an attempt to isolate it has been made.

DR. M. W. RUBENSTEIN: I am sorry that the bacillus has not been satisfactorily demonstrated. Nevertheless, I believe that all clinical evidence points definitely to leprosy as the diagnosis.

The acute exanthem which was present in May and June of this year has practically disappeared. The enlarged ulnar nerves, the alopecia of the outer portion of the eyebrows, the partial alopecia of the parietal and occipital regions, the atrophy of the thenar, hypothenar and interossei muscles of both hands, the loss of several digits of both hands and feet, the nodule on the bridge of the nose and the suggestive leonine facies are sufficient clinical evidence to support the diagnosis.

The patient's physician, in a small town nearby, was reluctant to accept the diagnosis. I shall, however, have more sections studied more carefully, and I shall try to obtain further nasal smears.

PELLAGRA. Presented by DR. M. W. RUBENSTEIN.

F. L., an unmarried woman aged 26, states that she was in excellent health until four years ago, at which time, while she was working in a store, a burglar held her up four times in one week. Immediately after that her appetite became poor and she began to suffer from nausea, vomiting and severe cramps. She weighed 145 pounds (65.8 Kg.) at that time. Since then she has taken no food other than milk. The patient has been under the care of a neurologist for the past year because of nervousness, spasms of the stomach, severe pain and colic. He made a diagnosis of paramyoclonus multiplex. The spasms included the abdomen and chest and were severe. Symptoms which had been present for the last four years have now practically disappeared. About five weeks ago a macular eruption occurred around the neck and inner aspects of the arms; this was followed immediately by an eruption on the dorsa of the feet and hands. The patient was unable to retain any food and vomited immediately after eating.

The patient is extremely emaciated; she weighs 83 pounds (37.6 Kg.). She presents a Casál necklace. Linear bands of dermatitis are present on the flexor aspects of the arms and forearms, and there is a mild exfoliative dermatitis of both hands, stopping sharply at the wrist. The dermatitis involves the tip of the nose. There is a linear band of dermatitis on the dorsa of the ankles, separated by a band of normal skin. There is also a band of dermatitis above the ankles. The patient complains that pain and swelling are present at times in the areas of dermatitis. There have been no vaginal, crural or perianal lesions or involvement of the mouth and tongue.

DISCUSSION

DR. G. J. BUSMAN: The case is interesting in that the manifestations add to the list of disorders due to mechanical or functional obstruction to normal ingestion of food. It is comparable to obstruction due to carcinoma, ulcer or similar involvement of the stomach. I do not think that the paramyoclonus multiplex was related to the pellagra, except so far as it interfered with nutrition.

DR. H. T. PHILLIPS, Wheeling, W. Va.: I have observed a somewhat similar disorder. The patient was given empirically one-half erythema dose of roentgen radiation on the wrists and marked improvement resulted. Vitamin and diet therapy, of course, were also used. Two years later it was learned that that patient had regained good health.

DR. M. B. GOLDSTEIN, Youngstown, Ohio: I believe that Dr. Rubenstein's patient also shows signs of hyperthyroidism.

DR. M. W. RUBENSTEIN: This case is particularly interesting to me because it represents one of the several at least precipitating factors in the cause of pellegra.

SUBACUTE FOLLICULAR DERMATITIS (VITAMIN A DEFICIENCY?). Presented by DR. G. J. BUSMAN and DR. F. A. HEGARTY.

G. S., a man aged 48, when first examined a month ago had a generalized follicular papular pruritic eruption. The skin had a distinct nutmeg grater feel. There were no lesions over the proximal phalanges. No systemic signs or symptoms were present. A Wassermann test of the blood, total and differential blood count, urinalysis and roentgen examination of the chest gave negative results. The patient's diet has been somewhat deficient but not abnormally so.

Biopsy showed chronic dermatitis and chronic folliculitis. The sections were not good, however; the lesion was a true dermatitis. It was nonsuppurative, was suggestively granulomatous, and involved the corium and hair follicles. There was very little change in the epidermis.

DISCUSSION

DR. F. M. JACOB: Infants exhibit a papular condition of the skin resulting from too much vitamin A. Conversely, there exists a condition arising from the lack of that vitamin. Dr. Pettler reported that two patients with pityriasis rubra pilaris improved on vitamin therapy. I wonder whether there is any relation between the two conditions.

DR. G. J. BUSMAN: The patient lived in a poor environment and on a poor diet. He reported at a hospital and was given a prescription for capsules containing vitamins A, B and D. He did not take the capsules, but he did correct his diet as advised, and improvement resulted.

PERSISTENT ERUPTION DUE TO IODIDE. Presented by DR. G. J. BUSMAN and DR. F. A. HEGARTY.

M. H., a woman aged 77, presents bluish-red, irregular nodules from the size of a split pea to that of a walnut on the fingers and on the extensor surfaces of forearms, elbows and legs. These lesions began to develop five years ago; since their appearance the patient has been subject to periodic attacks of a generalized papulopustular eruption.

When she was first examined by us, in November 1934, she presented the nodular lesions as described and a generalized inflammatory papulopustular eruption on the trunk and extremities. There was a history of recent ingestion of potassium iodide, and the history disclosed that the patient had been taking iodized salt for several years.

She was hospitalized and reacted severely to a test with 15 minims (0.92 cc.) of saturated solution of potassium iodide. The generalized picture responded readily to the intravenous injection of physiologic solution of sodium chloride. The nodular lesions which are present today have resisted all methods of treatment.

Examination of the urine for iodides gave negative results. The blood count showed 85 per cent hemoglobin, 4,020,000 red cells and 9,050 white cells. The results of the differential count were normal.

Biopsy showed focal chronic suppurative dermatitis and hypertrophy and hyperkeratosis of the epidermis.

DISCUSSION

DR. F. M. AMSHEL: The patient may be sensitive to iodides, but I think that the condition is xanthoma tuberosum multiplex. The color, consistency and location of the nodules point to that diagnosis.

DR. B. A. GOLDMANN: I agree with Dr. Amshel.

DR. J. J. HECHT: This patient had been at the Pittsburgh Skin and Cancer Foundation. At that institution a diagnosis of xanthoma tuberosum multiplex was made and verified by biopsy.

DR. H. T. PHILLIPS, Wheeling, W. Va.: Why could not the patient have had the two conditions?

DR. G. J. BUSMAN: I agree that the patient perhaps had exanthoma tuberosum multiplex, but when she was given the saturated solution of potassium iodide the lesions flared up, bullae developed and the mouth and tongue became sore. The patient herself knows that she is sensitive to iodides. The saline solution has brought the condition to its present state, but no further improvement can be achieved.

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## CLEVELAND DERMATOLOGICAL SOCIETY

J. R. DRIVER, M.D., *Reporter*

*Sept. 26 and Oct. 24, 1935*

H. J. MISKJIAN, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. W. H. CONNOR.

C. C., a woman aged 48, from the service of Dr. Cole and Dr. Driver at the City Hospital, has secondary syphilis and received seventeen injections of mapharsen, or a total of 860 Gm., from June 1934 to Feb. 20, 1935. In addition, she received twenty-five intramuscular injections of bismuth subsalicylate. A few days after the final injection of mapharsen was given, there developed a generalized pruritic eruption simulating seborrheic dermatitis. The patient was given sodium thiosulfate intravenously and by mouth and seemed to improve. The administration of bismuth subsalicylate was then resumed. The eruption, however, persisted, a moderate exacerbation and partial remission taking place. The patient has been hospitalized since Aug. 9, 1935.

There is a widespread scaly eruption consisting of erythematous patches with scales. The lesions are round, vary in size from that of a 5 cent to that of a 25 cent piece and have a tendency to spread at the periphery and to resolve at the center. Coalescence of some of the lesions presents an archiform contour. There is marked involvement of the palms and soles, associated with desquamation

The Wassermann reaction of the blood was strongly positive when treatment was started. On Oct. 5, 1935, it was 1 plus. The Wassermann reaction of the spinal fluid was strongly positive in June 1934 and again in September 1935; other results of examination were negative. The blood count showed 90 per cent hemoglobin, 4,880,000 red cells and 6,400 white cells with 70 per cent polymorphonuclears.

A biopsy was reported on as follows: "Minimal changes are present in the epithelium. There are some flattening of the rete pegs and hyperkeratosis. The corium shows a moderate amount of edema, and about the vessels is a scant infiltrate of small round cells of the inflammatory type."

### DISCUSSION

DR. H. J. MISKJIAN: In this case it would be difficult to rule out the possibility of an arsenical dermatitis, in spite of the fact that several months have passed since treatment with arsenic was given. There are certain features about the eruption which suggest the possibility of lymphoblastoma, especially the premycotic stage of mycosis fungoides.

DR. BENJAMIN LEVINE: A deposit of bismuth producing continued absorption might be responsible for this eruption. I have seen cases in which there was

an urticaria-like eruption which would clear up several weeks after administration of bismuth was discontinued. The eruption would return on resumption of bismuth therapy. I think that in this case the disorder may be regarded as an allergic eruption due to bismuth.

DR. J. R. DRIVER: Fixed eruptions following the administration of heavy metals are well known. Personally, I have never seen a fixed eruption quite as extensive as that which this patient presents. Eruptions of this type following the use of arsenic are often prolonged by subsequent injections of preparations containing heavy metals, such as bismuth and mercury. I am of the opinion that in this case the disorder is an eruption due to heavy metal which has been kept active by subsequent injections of bismuth subsalicylate.

DR. W. H. CONNOR: This patient has been studied from the standpoint of lymphoblastoma. Biopsy revealed none of the characteristics of that disease. Moreover, studies of the blood showed no abnormalities. Extensive cultures for fungi have also been made; all have given negative results. All administration of heavy metals has been discontinued, and the eruption persists, although it is possibly slightly improved. I wish to call attention also to the fact that the arsenical used was mapharsen.

DR. JOHN E. RAUSCHKOLB: I have observed this case since the appearance of the eruption, and I thought for a long time that the disorder was an arsenical dermatitis. I have also more recently thought that there was some suggestion of erythema multiforme or possibly of disseminating lupus erythematosus. Some injections of bismuth subsalicylate were given after the eruption appeared to see whether they accentuated the eruption. My co-workers and I were not sure that there was any particular exacerbation.

NOTE.—The patient died of bronchopneumonia in December 1935. Autopsy observations were not helpful in establishing a positive diagnosis of the cutaneous eruption.

A CASE FOR DIAGNOSIS. Presented by DR. JOHN E. RAUSCHKOLB.

N. T., a woman aged 65, single, from the outpatient department of the City Hospital, has a crusted crescent-shaped lesion, 4 cm. in length, on the lower portion of the left cheek. The lesion started three years ago as a small red spot which gradually increased in size. The patient picks at the lesion in order to remove crusts. Examination reveals also a perforated nasal septum and chronic ozena. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: One would have to consider the possibility of syphilis. However, the process seems to be rather superficial, and the configuration of the lesion and the history that the patient picks at it a great deal lead me to favor a diagnosis of dermatitis factitia.

DR. C. L. CUMMER: I have the same impression as Dr. Parkhurst.

DR. R. E. BARNEY: I also believe that this is possibly a case of dermatitis factitia on account of the rather acutely inflammatory base with crust formation and the presence of a certain amount of pus. I suggest that dressings moistened with boric acid be used in an effort to clear up the lesion; when it heals the real characteristics may be more apparent.

DR. JOHN E. RAUSCHKOLB: This patient was first seen about one week ago, and the biopsy specimen has not yet been examined. So much improvement has followed the administration of potassium iodide that in my opinion a diagnosis of tertiary syphilis is most probable.

NOTE.—Biopsy revealed a basal cell epithelioma, and the lesion healed completely after administration of fractional doses of roentgen rays according to the technic of Coutard.

ERYTHEMA PERSTANS. Presented by DR. R. E. BARNEY.

F. E. D., a man aged 36, states that five weeks ago an eruption appeared on the middle portion of the back. He had a similar attack in February 1935, which lasted for five months. This attack involved the middle third of the back. In the median portion of the back are four annular groups of papules varying in size from that of a 5 cent piece to that of a dollar. The borders of these patches are made up of rather superficial small pea-sized pink papules, while the centers are apparently normal skin. Outside the borders are a few similar, satellite papules. The Wassermann reaction of the blood was negative. The blood counts were normal.

A biopsy of material taken from the border of one of the patches revealed normal epidermis. In the corium, particularly in the reticular layer, there was an infiltrate made up of foci of cells of the lymphocytic series. These cells were disposed periglandularly and perivascularly and were uniform in size and shape. There were no mitoses and no plasma or giant cells.

The patient has been given salicylates by mouth.

DISCUSSION

DR. EMERSON GILLESPIE, Canton, Ohio: There is too much infiltration in these lesions to justify the diagnosis of erythema perstans. I favor a diagnosis of granuloma annulare.

DR. R. E. BARNEY: I have considered the possibility of granuloma annulare, but I do not think that there is enough infiltration, and histologically the section did not show the picture of that disease or of sarcoid.

SICKLE CELL ANEMIA WITH ULCER OF THE LEG. Presented by DR. E. W. NETHERTON.

B. H., a Negro aged 21, states that his father and mother and three brothers are living and well and that none of them has had any ulcers of the legs or chronic illness. Two years ago a small, crusted lesion appeared on the inner surface of the patient's right ankle. This developed into a chronic ulcer, lasting eight months. It then healed, leaving a soft, thin, pliable scar. In June 1934 a similar lesion appeared on the inner surface of the left ankle. This ulcer has not healed. Treatment has consisted of various local applications, eight roentgen treatments and some ultraviolet irradiation.

The patient is well developed and fairly well nourished. Just below the inner malleolus of the left ankle is an irregular, indolent, deep ulcer with well defined margins. The base is granular, grayish and covered with a purulent exudate. For some distance surrounding the ulcer the skin is hyperpigmented and slightly sclerotic. The scar on the right leg also shows hyperpigmentation at the border. There is no evidence of varicosity of the veins. The Wassermann reaction of the blood was negative. The blood count showed 2,900,000 red cells, 111,000 white cells and 58 per cent hemoglobin. The volume of packed red blood cells was 26 cc. per hundred cubic centimeters, 57 per cent of normal. There was moderate anisocytosis. The volume index was 0.98; the color index, 1.000, and the saturation index, 1.01. The results of the differential count were as follows: 52 per cent neutrophils, 37 per cent lymphocytes, 6 per cent eosinophils, 4 per cent monocytes and 1 per cent basophils. The icterus index was 4. The platelet count was normal. There was marked sickling of cells in fresh preparations after twenty-four hours.

The diagnosis was sickle cell anemia.

Treatment has consisted of dusting on of boric acid crystals followed by the application of dressing treated with petrolatum and oral administration of reduced iron and, for the past three weeks, of 10 drops of a saturated solution of potassium iodide.

The lesion has improved approximately 50 per cent under treatment.

DISCUSSION

DR. J. R. DRIVER: Sickle cell anemia is common among Negroes. I believe that every young Negro with chronic ulcer of the limbs of unexplained origin should have his blood examined for sickle cells.

TERTIARY SYPHILIS; DIFFUSE SYPHILOMA OF THE FACE. Presented by DR. W. H. CONNOR.

J. B., a man aged 57, from the service of Dr. Cole and Dr. Driver at the City Hospital, contracted syphilis in 1917 while he was in the army; he received fourteen injections in his arm. He was treated for erysipelas of the face in 1931. The patient states that he has suffered repeated injuries to his nose in his work as a structural iron worker and that his nose has been unusually large for several years. The present trouble started approximately six months ago with a scaly spot about the size of a 5 cent piece on the right cheek, and gradually similar lesions developed about the eyebrows and over the nose and upper lip in a more or less diffuse manner, producing marked swelling of the involved areas.

A roentgenogram revealed a striking infiltration of the tissues in the region of the eyebrows and forehead. The nose also shows this infiltrating process, and in addition there are dilated venules and occasional pustules over the tip of the nose resembling acne rosacea. The upper lip and to a certain extent the cheek present an edematous, erythematous infiltration and some areas of atrophy and scarring.

The Wassermann reaction of the blood was strongly positive. Examination of the spinal fluid gave negative results. Roentgen examination of the chest showed some calcified tuberculous scars in the region of the hilus of the right lung. There is no evidence of active tuberculosis. A test with a 1:1,000,000 dilution of tuberculin gave a 3 plus reaction.

Biopsy showed hyperkeratosis of the epithelium, and in the cutis, both in the papillary layer and in the deeper layers, were changes suggestive of tuberculosis. Tubercles were present, which tended to coalesce. There was evidence of central caseation in some of these areas. There was evidence in some areas of round cell infiltration about the vessels, and giant cells were present. The entire picture, however, was one of infectious granulation in which syphilis could not be ruled out. Stains for tubercle bacilli and Spirochaeta pallida gave negative results. The patient has received two intramuscular injections of 2 cc. each of iodobismitol and three intravenous injections of 0.3 Gm. each of neoarsphenamine.

DISCUSSION

DR. C. G. LA ROCCO: This patient was seen at the Charity Hospital about one month ago, just before his admission to the City Hospital. At that time his condition was considerably different, in that there was more acute inflammation and more edema. This process seemed to be chiefly demarcated about the mouth and chin, and there was evidence of some vesiculation on the surface. As there was a rise in temperature of over 1.5 F., it was believed that he had erysipelas superimposed on some other condition.

DR. I. L. SCHONBERG: The process, to my mind, corresponds to the rosacea-like tuberculid of Lewandowsky. At the border of the eruption one can demonstrate the apple jelly lesions characteristic of tuberculosis.

DR. R. E. BARNEY: I consider both syphilis and tuberculosis as possible diagnoses. Against the diagnosis of lupus vulgaris, however, is the fact that the process started too late in life and certainly would be unusual. Furthermore, I should expect to see more scarring if the disorder were tuberculosis. In favor of nodular gumma is the serpiginous outline of the eruption as well as the positive Wassermann reaction. I do not think that the disorder is acne rosacea-like

tuberculosis of Lewandowsky, for in that condition the lesions are considerably smaller. I suggest that in addition to preparations of bismuth and arsenic potassium iodide be administered.

DR. E. W. NETHERTON: I should subscribe to the diagnosis of syphilis in this case, and the response to the comparatively small amount of therapy given seems to bear out this diagnosis.

DR. C. L. CUMMER: I treated a patient with a disorder similar to this several years ago; the symmetry of the process resembled much that exhibited by Dr. Connor's patient. My patient's lesion was found to be a gumma and responded well to therapy.

DR. J. R. DRIVER: The case is interesting from the standpoint of differential diagnosis. In addition to the diseases that have been mentioned, I believe that clinically one would also have to consider the possibility of leprosy. The infiltration about the eyebrows is suggestive. However, I believe that the disorder is tertiary syphilis, and the positive Wassermann reaction and the response to treatment seem to make that diagnosis unquestionable.

DR. JOHN E. RAUSCHKOLB: The results of the biopsy are interesting. The presence of giant cell formation and infiltration suggesting characteristic tuberculosis illustrates the difficulty that is often encountered in differentiating histologically between tuberculosis and syphilis. The response to treatment during a period of less than two weeks has been remarkable and seems to establish the diagnosis of syphilis absolutely.

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## COMBINED MEETING OF THE DERMATOLOGICAL CONFERENCE OF THE MISSISSIPPI VALLEY AND CENTRAL STATES DERMATOLOGICAL SOCIETY

R. G. SENOUR, M.D., *Acting Secretary*

*Ninth Annual Session, Cincinnati, Nov. 16, 1935*

SAMUEL GOLDBLATT, M.D., *in the Chair*

### ERYTHROPLASIA OF QUEYRAT?*

I. H., a Negro aged 38, states that he has had gonorrheal urethritis since 1915. In 1928 he had an acute retention, which was relieved by catheterization. In 1931 he underwent a suprapubic cystotomy. Since 1929, the prepuce and the glans penis have been inflamed.

Before that the patient had no penile lesions of any sort, and he has had no generalized eruption. In 1925 he had a bubo on the right side, which was incised and drained. No history could be obtained of intramuscular or intravenous therapy of any sort and there is no history of syphilis. At various times the patient has undergone incision and drainage for perineal and scrotal abscesses, and in 1932 he had a prostatic abscess.

The cartilaginous-like swelling and redness have remained about the same for the past three years; the inflammation of the glans seems to improve at times.

The Kahn test of the blood has been repeatedly negative. A smear from material from the glans showed no organisms. Dark-field examination and the Frei test gave negative results.

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* This and the following presentations were made by members of the dermatological staff of the Cincinnati General Hospital or by members of the Cincinnati Dermatological Society.

Biopsy revealed irregular areas of acanthosis, vacuolation of epidermal cells, chiefly in the prickle cell layer, infrequent mitoses, infiltration of lymphocytes and plasma cells in the upper portion of the derma and slight perivascular lymphocytic infiltration.

Therapy has consisted of local dressings with mild medicaments.

DISCUSSION

DR. S. S. GREENBAUM, Philadelphia: I suggest an alternate diagnosis of granuloma inguinale limited to the glans penis. The marked induration present in certain areas of the lesion does not conform to the clinical description of erythroplasia. I think it may be well to make a therapeutic test with freshly prepared antimony and potassium tartrate.

DR. RICHARD S. WEISS, St. Louis: In examining the sections I thought I could detect many of the features that are described as occurring in erythroplasia of Queyrat. My co-workers and I have a white patient, aged about 38, who has a similar process; in his case there is not quite as much inflammation, but the histopathologic features are quite similar to those exhibited by this patient. There are acanthosis and breaking through the basement membrane and a moderate subepidermal inflammatory infiltration. I believe this patient's disorder will turn out to be erythroplasia of Queyrat, and, in my opinion, unless the penis is amputated and the inguinal glands are cleaned out, the prognosis is highly unfavorable.

DR. MARION B. SULZBERGER, New York: I agree with the remarks of Dr. Weiss, but I should caution against making this diagnosis without both clinical and histopathologic evidence. I think that not infrequently one sees lesions of the penis which simulate erythroplasia. Not all these lesions turn out to be this rather rare condition. One must therefore exercise great care in making the definite diagnosis and in considering the indications for radical therapy. Not only the clinical and histologic appearance but the characteristic course are essential to the diagnosis. Nevertheless, in this case I agree with Dr. Weiss; the clinical history and the clinical and histopathologic picture are all consistent with the diagnosis of erythroplasia of Queyrat.

SCLERODERMA WITH SCLERODACTYLIA; HORNER'S SYNDROME FOLLOWING CERVICAL GANGLIONECTOMY.

Mr. F. R., aged 47, is presented through the courtesy of the department of peripheral vascular disease of the department of surgery, Cincinnati General Hospital.

He was first admitted to that hospital in 1931. According to the history, the disorder appeared in 1912, beginning as numbness, tingling, cyanosis and cramping of the fingers. Each year thereafter the symptoms seemed to increase in severity and extent, the reactions being less intense in the toes. The patient fell on the right hand in 1931 but suffered no fracture. At that time the entire hand showed extensive cyanosis and partial flexion contracture of the right index finger; there was similar cyanosis, though less marked, in the feet. Sensation was entirely normal at that time.

The patient said that he used tobacco moderately, smoking one package of cigarets every three or four days. He stated that he did not have syphilis. He had gonorrheal urethritis at 17 and at 22.

In 1931 the entire left stellate ganglion and part of the last cervical and the second dorsal ganglion were removed by Dr. Reid and Dr. Zinninger. Immediately after the operation it was noted that the left side of the face and forehead were not sweating. Several hours afterward the left hand became definitely pinker and warmer than the right. Constriction of the pupil was noted the next morning. The blood pressure in the right arm was 104 systolic and 68 diastolic; in the left arm it was 118 systolic and 70 diastolic. On admission some calcification of the pleura was found. There were no other abnormalities. Five or six

months after the operation the patient was reexamined and found to be free from symptoms in a portion of the left side, but there were pain, coldness and discoloration in the right hand and in both feet. The Horner syndrome at this time was also rather marked. Measurements of the cutaneous temperature at this time showed an increased temperature on the left side, starting approximately at the middle of the forearm. There was a difference in temperature of 4 or 5 F. In 1933 the patient was readmitted, and at that time it was noted that he had some trophic changes about the fingers of the left hand and that the changes in the forearms were more marked. The calcium content of the blood was 11.8 mg. per hundred cubic centimeters, and the phosphorus content, 4.2 mg. No changes were noted in the bones of the hand. The patient received 2 cc. of a 0.1 per cent solution of pilocarpine hydrochloride hypodermically daily only for about seventeen days, but no improvement resulted.

There is no family history of Raynaud's disease, tuberculosis or syphilis.

The skin shows changes in the extremities as noted. In addition, sclerodermic facies seems to be developing.

Physical examination gave negative results except for chronic prostatitis.

No laboratory examinations have been made recently; studies of the blood when made gave negative results.

No biopsy has been made.

The condition appears to be becoming progressively worse.

Recently treatments with hyperthermia have been employed, but no improvement has resulted.

DISCUSSION

DR. I. J. ARNSSON, Buffalo: In the light of the investigation by Sellei, of Budapest, Hungary, it seems advisable to keep these two concepts separate: that of true scleroderma and that of what he called acrosclerosis (sclerodactylia). The etiology, prognosis and treatment of the two conditions are quite different. Whereas scleroderma is thought to result from a disturbance of the glands of internal secretion, particularly the pancreas, sclerodactylia, or acrosclerosis, is a vascular disease and has no relation to the endocrine glands. In the majority of Sellei's cases of scleroderma the utilization of glandular therapy proved to be successful, whereas the same treatment was entirely unsuccessful in cases of sclerodactylia, or of what he called acrosclerosis. There are some features and laboratory tests which make possible the differential diagnosis of the two diseases.

DR. FRED WISE, New York: I should like to hear the presenter's opinion of the interpretation in more definite terms than the history gives. He used the term scleroderma. I was unable to find any true scleroderma. I saw an acro-asphyxia. Sellei described this condition under the name of acrosclerosis, but I did not see much acrosclerosis in this case. My co-workers and I use the term acro-asphyxia for this type of condition and I think that is related to Raynaud's disease.

DR. LEON GOLDMAN, Cincinnati: Recently changes have developed in the face. Palpation of the cheeks shows that the tissues are much more firm than previously. The changes in the forearm have appeared within the last three or four years, and there are changes in the leg, extending to the foot. The changes in the skin include some atrophy. The Horner syndrome has appeared after the ganglionectomy; there is definite miosis of the pupil.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: In my opinion this condition is to be considered as distinct from true scleroderma; it represents a form of symmetrical vasospastic disturbance of the extremities of unknown etiology which Sellei named acrosclerosis. Raynaud's disease in male patients is extremely rare. When patients with extensive scleroderma were subjected to treatment by sympathetic ganglionectomy my colleagues and I were at first rather optimistic about the degree of benefit that was obtained. Subsequent observation revealed, however, that such radical treatment is hardly justified unless there is a definite preponderance of the Raynaud syndrome.

SCLERODERMA; ACNE ROSACEA.

Mrs. M. M., aged 34, says that in the early part of 1934 she first noticed on the left thigh a brownish area; this gradually became firmer and soon became devoid of hair. Shortly afterward a similar eruption appeared on the right thigh and on the lower portion of the legs. At the time of admission to the hospital the patient was about three months pregnant. The rosacea had been present for a number of years, periods of exacerbation being associated with the menses and occasionally with certain dietary indiscretions.

The skin shows rosacea of moderate intensity. There are brownish firm atrophic areas 4 by 6 cm. on the anterior surfaces of both thighs, the disorder being less marked on the lower portion of the legs. Small patches are present also on the abdomen and on the back of the neck.

Physical examination showed prominent eyes; the thyroid was diffusely palpable; there were no thrills and no tachycardia or other abnormalities.

Urinalysis, the Kahn test, blood counts and differential counts gave normal results. The basal metabolic rate was +2 per cent. Dextrose tolerance tests showed slightly increased tolerance. Roentgen examination of the sella turcica showed no abnormality.

Biopsy showed changes typical of scleroderma.

In spite of the pregnancy, endocrine therapy, with preparations of the thyroid gland, ovaries and pituitary gland was given cautiously for several months, without any results. Treatment of each leg with the inductotherm produced no appreciable results. The patient was then given four treatments with the Kettering hypertherm, the temperature being maintained at from 104 to 105 F. for twenty hours. After these treatments there was definite improvement, the lesions becoming much softer. As pregnancy became more advanced it was considered advisable to discontinue all forms of therapy. The patient was delivered of a normal child in October 1935. Since that time she has received no treatment.

DISCUSSION

DR. RICHARD S. WEISS, St. Louis: I was interested in hearing one of the speakers say that in his experience endocrine therapy cures scleroderma. In my experience results have not been as satisfactory. I have seen certain disorders, particularly the localized and morphea types, clear up as a result of treatment with thyroid, but, on the other hand, I have seen the disorders clear up without any treatment or fail to clear up with treatment by any method. I should like to hear Dr. Arnsson discuss this more fully.

DR. I. J. ARNSSON, Buffalo: I was referring to the experience of Sellei, not to my own.

DR. FRED WISE, New York: I think it is worth while reporting to the members that Sellei at the recent congress in Budapest, Hungary, presented at least three patients with scleroderma who, judging from the histories, did get well as a result of his treatment. He gives not only pancreatic extract but also desiccated stomach and a "shotgun" preparation of iron, mercury and other heavy metals. There is no definite therapy except the administration of pancreatic extract. I was impressed by the cases of scleroderma that Sellei presented. I did not perceive favorable results in cases of Raynaud's disease or of acrosclerosis.

DR. MYER W. RUBENSTEIN, Pittsburgh: At present my co-workers and I have under observation a patient with generalized scleroderma who has apparently responded to treatment with pancreatic extract. Several months ago this patient presented a generalized scleroderma, and the prognosis at that time was unfavorable. Treatment has consisted chiefly of administration of pancreatic extract orally and an insulin-free pancreatic extract intramuscularly. The response has been favorable. At present there is only a moderate degree of acrosclerosis in both hands.

PRURIGO NODULARIS.

M. G., a Negress aged 54, states that lesions first appeared on the lower portion of the legs thirty years ago and have gradually spread and increased in number until at present the eruption involves all the cutaneous surfaces. There are no lesions on the mucous membranes.

The patient's father and mother never had a cutaneous disorder. She had eleven brothers and sisters; seven lived to adult life. Only one brother had a cutaneous condition. His arms itched intensely at times, but no eruption ever appeared.

The patient is well developed and well nourished and is apparently in good health. Scattered over the arms, legs and trunk are numerous hard elevated intensely pruritic nodules and papules from the size of the head of a brass pin to that of a large pea. The smaller lesions are skin-colored and slightly pigmented and have a smooth surface; the larger ones have a verrucous surface and are a darker brown than the normal skin. There are a few scattered lesions on the scalp. No lesions are present on the mucous membranes. There are no other abnormalities. Palpation and auscultation show the heart, lungs and abdominal viscera to be normal.

The Wassermann reaction of the blood was negative. The sugar content of the blood was 112 mg.; the calcium content, 10.2 mg., and the nonprotein nitrogen content, 36.3 mg. per hundred cubic centimeters. Urinalysis showed an acid reaction, a specific gravity of 1.018 and no albumin, sugar or indican. Microscopic examination of the urine showed a few leukocytes and epithelial cells and acid phosphates.

Biopsy of material from large and small nodules showed the following changes: hyperkeratosis; acanthosis; irregular proliferations of rete pegs; large masses of new connective tissue in the corium, most of which had formed around small blood vessels; some hyaline degeneration of collagen and loss of elastic tissue; moderate cellular infiltrations consisting chiefly of lymphocytes, with a few polymorphonuclears, around the vessels, and hyperplasia of the intima of small vessels with partial obliteration of the lumen.

In sections from the normal skin the epidermis appeared normal. In the corium there was some hyaline degeneration of the collagen with formation of new connective tissue. Slight perivascular infiltration with lymphocytes and occasional polymorphonuclears was present.

The cutaneous condition has remained unchanged in spite of treatment, except for transient patches of "eczema" that have appeared on the legs and an occasional papule that appears to become absorbed.

The patient states that six years ago she received injections of sodium iodide, mercury succinimide and neoarsphenamine. The latter drug relieved the pruritus and "weak spells" to which the patient was subject, and it caused some of the spots to disappear. Large doses of calcium and viosterol brought about a lessening of the pruritis, but none of the nodules underwent any change. Freezing the nodules with carbon dioxide snow caused exfoliation of the tops of the lesions but no other change. Thorough desiccation of the nodules caused their temporary disappearance, but they recurred in a few months. Roentgen radiation in doses of from 1 to 3 skin units had no effect on the lesions. Injections of from 0.45 to 0.6 Gm. of neoarsphenamine every week or two produced relief from the pruritus and was followed by apparent disappearance of a few lesions.

DISCUSSION

DR. WILLIAM H. GUY, Pittsburgh: I hesitate to make a suggestion as to investigation in a case of prurigo nodularis on the basis of one observation which my co-workers and I were not able to follow up, but in a case of a similar disorder in the course of the routine physical examination visualization of the gallbladder showed a number of impacted stones. There were no symptoms referable to the biliary tract. I have always wanted to investigate another case

of that kind to see whether there was disturbance of the biliary tract, not necessarily a stone but disease in that region, the correction of which might produce some relief.

DR. FRED WISE, New York: One does not often see conditions like this, and I think that they should be discussed. Pautrier recently wrote a good description of a condition in which he demonstrated nerve fibers within the lesion, so this disorder and Recklinghausen's disease seem to be two diseases in which one can actually demonstrate nerve fibers in the primary lesion. That histologic demonstration may account for the itching present in this condition.

DR. S. W. BECKER, Chicago: Cases of prurigo nodularis are always interesting because of the two opinions concerning them, namely, (1) that the disorder always starts with itching and the patient produces the nodules by scratching, and (2) that the nodules appear first. I questioned this woman carefully, and she stated definitely that the itching appeared first and the lesions came afterward, which supports the idea of French authors that the lesions are neurogenic.

POIKILODERMA (JACOBI).

Mrs. C. A., aged 52, was apparently normal until the present condition appeared on the anterior aspect of the thighs thirty-one years ago. Since then it has progressively spread, and at present it affects the greater portion of the body, but the hands and face are only slightly involved. The skin is pruritic and burns at times. The symptoms are worse in winter than in summer. The patient has had "heart trouble" for the past ten years; she has suffered from chronic constipation all her life, and she has constant headaches in the parietal region. Menstruation is normal and regular. The skin appears to clear up during menstruation. The patient states that she has had no venereal infection; she induced two miscarriages, one at 18 and one at 19.

Scattered over the trunk, neck and extremities, especially on the adductor surfaces, is a diffuse mottled macular pigmentation of the skin, which appears dry and in many places resembles a mild roentgen ray dermatitis. Close examination shows dilatation of the superficial capillaries, with many bright red cayenne pepper spots. Areas of distinct atrophy of the skin appear as white spots in a retiform network of hyperpigmentation. There are numerous small scars on the skin, resulting from scratching and from previous infections.

Physical examination showed that the patient was well developed and well nourished; she presented no evidence of muscular atrophy and was not apparently ill. The pupils were irregular but reacted to light; other reflexes were normal. The buccal mucosa was normal. The heart was not enlarged; no murmurs were heard, and the rate and rhythm were normal. The blood pressure was 135 systolic and 80 diastolic. The lungs were normal. Palpation of the abdomen showed no abnormal masses or areas of tenderness. The glands were not enlarged. Pelvic examination gave negative results. The vaginal mucosa was normal.

The Wassermann test of the blood and urinalysis gave negative results. The blood count showed 4,300,000 erythrocytes, 6,200 leukocytes and 85 per cent hemoglobin. The differential count showed 72 per cent polymorphonuclear neutrophils, 24 per cent lymphocytes and 4 per cent eosinophils. Roentgen examination of the pituitary fossa showed normal conditions.

Biopsy of material from an atrophic area of the skin showed hyperkeratosis, absence of the stratum lucidum and stratum granularum, flattening of the stratum mucosum with loss of rete pegs, fragmentation and degeneration of the collagen and degeneration of the elastic tissue in the papillary and reticular layers; dilatation of capillaries and lymphatics and a rather diffuse infiltration of lymphocytes in the corium.

During the three years the patient had been under observation her condition had remained unchanged. At one time while she was receiving ultraviolet radiation there appeared numerous pruriginous papules from the size of a pinhead to that of a pea, which biopsy showed to be lymphocytic granulomas.

Because of lack of involvement of the exposed portions of the skin the patient was given repeated treatments with ultraviolet radiation, but no improvement in the cutaneous condition resulted. Roentgen irradiation of the acutely pruritic

papules caused their prompt disappearance. Solution of potassium arsenite caused aggravation of the pruritus and increase in the number of papules.

DISCUSSION

DR. WINSTON RUTLEDGE, Louisville, Ky.: I first saw this patient about three years ago; at that time she presented practically the same picture she now exhibits, except that at varying intervals since then a number of intensely pruritic papules have developed on the trunk and extremities. Histologic examination of one of these papules showed only a dense lymphocytic infiltration in the corium. I treated some of these lesions with roentgen radiation, and some cleared up spontaneously. The histologic studies confirmed the diagnosis of poikiloderma.

DR. JAMES M. MARKIN, Rochester, N. Y.: I did not notice much atrophy or much telangiectasia in this case. In spite of the history of long duration I think that a diagnosis of mycosis fungoides should be considered. The patient had a pruritic eruption for a number of years, and then this trouble developed. I think that the possibility of parapsoriasis might also be considered. However, in my opinion, the response of the nodules to roentgentherapy and the results of the histologic examination are suggestive of mycosis fungoides.

DR. WILLIAM H. GOECKERMAN, Los Angeles: About fifteen years ago I saw a patient with a condition that was rather puzzling, and I looked up the first report that Jacobi made. The condition exhibited by our patient was an exact duplicate of that described by Jacobi. Since then I have been on the lookout for additional cases of the disorder, but I have seen only two. One of these was shown to me by Professor Jadassohn, and the picture was classic. It will be recalled that when he saw Jacobi's case he favored a diagnosis of lupus erythematosis but later rescinded that diagnosis and agreed with Jacobi. I realize that the tendency has always been to include other disorders in the poikiloderma group. For instance, in Chicago in 1933 a number of cases were shown of a rather bizarre eruption classified as poikiloderma, but if one adheres to Jacobi's description I think that one cannot diagnose the condition in any of these cases as poikiloderma. The picture is difficult to describe, but once one has seen a typical manifestation I think it is hard to confuse the condition with anything else. In this case I suggest the diagnosis of pityriasis lichenoides chronica.

DR. H. R. FOERSTER, Milwaukee: The discussion brings up the old controversial question regarding the interpretation of poikiloderma. Do the cutaneous lesions presented by this patient represent a pathologic entity or merely objective symptoms of a transitional stage of some other chronic dermatosis? The atrophic reticulated pigmented lesions presented by this patient suggest to me the clinical picture of the condition known as poikiloderma atrophicans vasculare. The infiltrated, exudative plaques on the back suggest the possibility that this condition belongs to the lymphoblastomatous group, with the picture of poikiloderma making up one phase of the symptomatology and the plaquelike lesions possibly representing beginning tumor formations of the mycosis fungoides type.

AMYLOID DISEASE OF THE SKIN.

Mr. J. B., aged 50, states that lesions appeared on the legs in the early part of 1933, after an infection of the upper portion of the respiratory tract. No lesions were present elsewhere on the body. No history of any previous cutaneous lesions of any sort could be elicited.

Physical examination gave essentially negative results.

Both legs are covered with hypertrophic polygonal brownish-red papules, the eruption being most marked on the anterior aspect. The upper extremities are not affected; the mouth shows no abnormalities.

The Kahn test and urinalysis gave negative results. The cholesterol content of the blood was 133 mg. per hundred cubic centimeters. The congo red test gave normal results.

Staining of biopsy material with iodine green disclosed irregular amyloid masses scattered throughout the papillae.

The patient has received 2 erythema doses of roentgen radiation in divided dosage, solution of potassium arsenite and yellow mercurous iodide.

There have been repeated infections of the leg following excision of material for biopsies; otherwise no change in the condition has occurred.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Dr. Nomland has recently perfected a simple and interesting technic for the demonstration of amyloid in the skin in vivo. A small amount of a 1 per cent aqueous solution of congo red is injected subcutaneously in the vicinity of the suspected lesions. If amyloid is present it takes up the dye selectively during the next few hours, and the lesions assume a reddish hue, which persists for many days or even months. My colleagues and I recently observed a case of systematized amyloidosis in which the zones of amyloid in the skin became stained selectively after the dye was injected intravenously according to the technic of Paunz for estimation of possible visceral involvement.

DR. R. G. SENOUR, Cincinnati: The congo red stain was tried on this patient's lesions, but there was no retention of the stain.

DR. HOWARD J. PARKHURST, Toledo, Ohio: From the clinical standpoint the lesions impressed me as resembling lichen planus ocreaformis. Lieberthal wrote a paper on this subject a number of years ago.

DR. J. EDGAR FISHER, Cleveland: About two years ago (ARCH. DERMAT. & SYPH. **26**:586 [Sept.] 1936) I presented before the Cleveland Dermatological Society a patient with lesions over the extremities; the disorder was diagnosed as lichen planus ocreaformis, and it was quite similar in appearance to that exhibited by this patient. The condition is described in Sutton's textbook.

DR. R. G. SENOUR, Cincinnati: This patient was presented before the Cincinnati Dermatological Society a year ago with a diagnosis of lichen planus ocreaformis of Lieberthal, but when my colleagues and I saw the patient a month ago we called the disorder a mutation to amyloidosis.

PSEUDO-ATROPHODERMA COLLI.

Miss E. K., aged 41, states that her cutaneous disorder began in 1927, the lesions appearing at first as some scaliness about the base of the neck. A few months afterward peculiar lattice-work bands were noted. This condition seemed to be spreading gradually along the shoulders and down the back and chest. No subjective symptoms of any sort have been present. The patient is certain that at times the condition seems to be much less obvious than at other times. She can assign no reason for this difference. Her general health is good. Some vague discomfort in the right upper quadrant of the abdomen has been diagnosed as cholecystitis by her attending physician. She underwent an appendectomy a few years ago. There have been no previous cutaneous disorders.

The skin is warm, moist, elastic and exhibits a moderate degree of dermographism. The lesions show a diffuse redness and scaliness. The involved area seems to be made up of circular depressions covered with bluish-red, linear markings. Along the periphery are radiating spots of smooth brownish skin, which at a casual glance resemble the lesions of pityriasis versicolor. Tension on the skin seems to obliterate the lesions somewhat.

General examination, including examination of the fundi, gave entirely negative results; the blood pressure was 130 systolic and 92 diastolic.

Repeated examinations of scrapings of skin for fungi, urinalysis and the Kahn test gave negative results.

Biopsy revealed slight thinning of the epidermis, rete plugs and papillae; there was sparse lymphocytic infiltrate scattered throughout the upper portion of the

corium; the Verhoeff eosin, Van Gieson and Foot-Foot stains showed no disturbances of the collagenous and elastic tissue.

The patient received treatment for a few months, but no appreciable change in the appearance of the lesions resulted. In August 1935 the lesions were definitely improved; at that time the patient was receiving no treatment of any sort. The area has not been exposed to the sun.

Treatment has consisted of local massage and administration of thyroid gland preparations.

DISCUSSION

DR. S. W. BECKER, Chicago: This patient's condition corresponds in every detail to that which Dr. Muir and I described (ARCH. DERMAT. & SYPH. **29**:53 [Jan.] 1934) under the name of pseudo-atrophoderma colli. This patient's lesions are more extensive and more evident than any I have seen. There are evidently slight epidermal atrophy and a loss of elasticity, which account for the smoothness of some of the plaques and the cigaret-paper crinkling between the smooth plaques. One case which I observed many years ago in Dr. O'Leary's service at the Mayo Clinic was reported by Dr. Jeffrey Michael, who stated that complete restoration to normal occurred after many years; this makes me believe that there is no real dermal atrophy in this condition.

DR. ELMORE B. TAUBER, Cincinnati: In this case, as in that which Dr. Becker and Dr. Muir reported, the lesions are generally worse in winter; in fact there have been periods in the summer when there was no atrophy or shininess and the skin looked practically normal.

DR. RICHARD S. WEISS, St. Louis: I suggest that the diagnosis of pseudoxanthoma elasticum be considered in this case.

DR. JACK JONES, Atlanta, Ga.: When I examined this patient the light was not very good, but I tried to find the features of pseudoxanthoma elasticum. She states that she had a definite ocular disturbance. My colleagues and I have seen twelve or fifteen cases of pseudoxanthoma elasticum associated with angioid streaks of the retina, and I wonder whether in this case angioid streaks are not present also.

DR. ISADORE ROSEN, New York: Dr. Tauber said that in the summer the lesions disappear. I cannot understand how areas of skin affected by dermatosis with atrophy can regenerate. I suggest the diagnosis of tinea versicolor, and I think that repeated examinations should be made for Microsporon furfur because one occasionally sees patients with this infection whose lesions clinically give the appearance of atrophy.

DR. HOWARD J. PARKHURST, Toledo, Ohio: Many of these lesions show follicular plugs, and I think that the diagnosis of lichen planus atrophicans should be considered.

## A CASE FOR DIAGNOSIS.

Mrs. G. G., aged 26, has been presented at various dermatological conventions throughout the country in the past five or six years, exhibiting some of the various phases of her condition. No definite diagnosis has been made. The cutaneous lesions appeared approximately one year after birth. The picture has varied from that of dermatitis exfoliativa to that of a skin almost normal except for discrete scaling erythematous patches. Occasionally the patient complains of subjective symptoms of pruritus and burning, but there are no other disturbances.

There is no family history of psoriasis. Physical examination gave essentially negative results. Few discrete areas are visible at the present time.

The Wassermann test, urinalysis, determination of the sugar and urea content of the blood and blood counts gave normal results. No eosinophilia was present on repeated smears.

One biopsy was reported by Dr. Goeckerman to show psoriasis.

There has been practically no change in the condition during the period of observation. During the early part of a pregnancy the skin seemed to clear up, but the condition recurred during the later part of the pregnancy.

Numerous treatments of all sorts, including courses of sodium thiosulfate therapy, intravenous administration of a preparation of thyroid, medication with calcium, various types of diets and local application of coal tar have been used. At present the patient is receiving treatment with the Kettering hypertherm.

DISCUSSION

DR. ELMORE B. TAUBER, Cincinnati: If it is true, as the patient maintains, that at times her skin has been clear, I should accept the diagnosis of psoriasis; but I have had the patient under observation for ten years and have never seen her skin clear. At present there is some improvement, and the disorder seems to be psoriasis. A biopsy made at the Mayo Clinic indicated psoriasis. I think, however, that the condition belongs in the group that resembles psoriasis and the parapsoriasis of Brocq. Subjective symptoms are absent most of the time. The disorder has been present in five generations. The patient has a child that is now about 2 years old and shows no signs of cutaneous eruption. Each member of the patient's family has exhibited this disorder about six months after birth.

DR. WILLIAM H. GOECKERMAN, Los Angeles: I now remember seeing this patient about six years ago, but I did not recognize her at first. I recall that my co-workers and I had an opportunity to study the patient at some length. My first thought was that we might be dealing with pityriasis rubra pilaris, but after examining the patient carefully again I am willing to subscribe to the diagnosis of psoriasis.

DR. FRED WISE, New York: During the past ten or fifteen years at least half a dozen cases of linear or striate psoriasis have been presented in New York, in all of which it was stated that the lesion appeared in infancy or in childhood. I am firmly convinced that psoriasis may appear in the form of a nevoid lesion, and I think that this is an example of nevoid psoriasis. I have encountered linear lichen planus manifested as a nevoid lesion of unilateral type.

DR. I. J. ARNSSON, Buffalo: One would expect psoriasis to produce more characteristic signs. My colleagues and I were unable to find any bleeding from capillaries. In my opinion the histologic picture in this case is more like that of parapsoriasis than like that of psoriasis. I should expect more parakeratosis than is present. Slight parakeratosis and pronounced hyperkeratosis are present, and that argues against the diagnosis of psoriasis.

DR. LESTER HOLLANDER, Pittsburgh: I think I saw this patient four or five years ago, but at that time the eruption was much finer. The point Dr. Arnsson brought out about pinpoint bleeding was one of the things that made me think at that time that the condition was psoriasis, and today I am convinced that that diagnosis is correct. The lesions are more typical now. I believe that many of the changes present are due to the great amount of treatment the patient has received. I think she should be sent to the seashore if possible; that would do her more good than any form of therapy.

DR. RICHARD S. WEISS, St. Louis: I agree with the members who think that this is a case of psoriasis, and I wish to call attention to the point that Engman and McCarry brought out years ago, namely, that fever may cause psoriasis to involute. It does not clear it up permanently of course. I think the point brought out by Dr. Tauber confirms the diagnosis of psoriasis as well as the other points that have been brought out so far.

DR. HOWARD J. PARKHURST, Toledo, Ohio: I found a few pits on the nails, and the condition of the scalp, I think, confirms the diagnosis of psoriasis.

DR. NORMAN TOBIAS, St. Louis: I saw this patient about two years ago, after the birth of her baby, and the preliminary diagnosis then was paraspsoriasis. When she was examined more carefully typical lesions of psoriasis were found on the

lips and nose. The biopsy specimen was typical of psoriasis. Her pregnancy apparently had no effect on the appearance of the lesions. I recall definitely that neither ultraviolet irradiation nor local applications had any effect on the lesions.

### Ichthyosis Hystrix.

H. H., a boy aged 13, has had the present cutaneous condition since birth. There is marked dryness of the skin, and it is scaly, so-called "fish skin." Ulcers frequently develop on the hands or feet.

The patient's father has pulmonary tuberculosis. Except for that, the family history is irrelevant.

The skin shows generalized thickening, and there is a marked desquamation, giving a fish-scale appearance. Superficial ulcers are present on both wrists, knees and ankles and on the abdomen.

Physical examination gave essentially negative results except for a purulent discharge in the left ear. The tonsils were hypertrophied and inflamed. There was serous discharge from the nose.

The Wassermann test and urinalysis gave negative results. Examination of the blood showed 4,500,000 erythrocytes and 11,000 leukocytes. The differential count gave the following results: polymorphonuclears, 68 per cent; lymphocytes, 25 per cent; mononuclears, 5 per cent, and transitionals, 2 per cent. The basal metabolic rate averaged + 4 per cent on three different tests.

Biopsy revealed marked hyperkeratosis and occasional areas of parakeratosis; pyknosis and vacuolation of basal cells and a decrease in the number of prickle cells; lymphocytic and polymorphonuclear infiltration; a sparsity of blood vessels, a few of the vessels present being dilated, and some increase in collagenous tissue.

The condition is the same as it was when the patient was admitted to the hospital.

No treatment has been given.

#### DISCUSSION

Dr. Richard S. Weiss, St. Louis: I suggest a diagnosis of congenital ichthyosiform erythroderma. The patient has a reddened skin and ichthyotic patches. The ichthyotic manifestations are not thickest on the sites where ichthyosis ordinarily occurs, namely, the extensor surfaces of the forearms, arms, legs and thighs; on the contrary, they are thickest about the joints, particularly about the elbows and knees, and there are lesions about the axillary folds and the buttocks. The condition is, I think, the dry form of congenital ichthyosiform erythroderma. In addition, the patient exhibits the dry scaly scalp so often associated with this disease.

Dr. Howard J. Parkhurst, Toledo, Ohio: I think that the disorder is congenital ichthyosiform erythroderma with formation of bullae. The crusted lesions are suggestive of that condition.

### Milroy's Disease.

(This case was reported by Dr. McGuire and Dr. Zeek in *The Journal of the American Medical Association* (**98**:870 [March 12] 1932.)

Mr. M. W., aged 21, in 1926 first noticed swelling of his legs, not associated with a systemic reaction. Recently, however, he has been repeatedly hospitalized because of febrile episodes. In 1930 the Kondoleon operation was performed by Dr. Reid, the procedure being described as follows: "Incision was made from just below the greater trochanter down to the external malleolus. In the thigh about one-half inch of skin was removed and below the knee a little less than this amount. After getting through the skin and little subcutaneous tissue the flaps were widely undermined, both above and below the knee. This was carried to a point beyond which we were afraid that circulation to the edges of the flap would be impaired. A large amount of the subcutaneous fat and fascia and the fascia of the muscles were removed from above and below the knee. Below the knee one was par-

ticularly struck by the dense fibrous tissue and the very large lymphatic spaces. Cutting into some of these lymphatics was like cutting into small serous cysts. Below the knee the fascia was removed from the midline anteriorly to the midline posteriorly and a great deal of scarred subcutaneous tissue and fat along with it. The scarring down over the lymphatics was not nearly so prominent above the knee as below. During the operation, some of the tissues were taken for culture. Bleeding points were ligated with silk and the wound closed with interrupted medium silk sutures throughout without drainage."

This operation gave the patient slight relief, but even after this the acute episodes continued. He also showed evidence of pituitary dyscrasia with possibly Fröhlich's syndrome. Roentgenograms of the legs showed a considerable network of shadows. The bones remained normal.

There is a fairly definite history as far back as the grandfather, who had swollen legs. The grandfather married twice; his first wife bore two daughters. One died in infancy, of unknown cause; in the second, edema of the legs developed at puberty. Her children, two girls, were likewise affected with edema of the legs at puberty. By his second marriage several children were born, but information was obtained about only two of them. Both were males and had swelling of the legs, which began at about the fourteenth year. One, the father of the patient, has been married twice. By his first wife two children were born; these remained normal; one is 30 and the other 35 years of age. By his second wife two children were born, the patient and his brother. Both have edema of the legs. The father of the patient has had acute attacks, first at the age of 14, consisting of swelling in the right groin associated with malaise, chills and fever. He has exhibited swelling of the entire right leg, redness, tenderness and pain, followed after several days by increase in the size of the legs and desquamation. He has had a hundred or more of these attacks. A half-sister of the patient's father has had more frequent and more severe attacks.

The patient's heart and lungs are normal. The visual fields are normal.

The condition is limited to the lower extremities. There is enormous edema of the ankle and leg between the knee and the ankle. The edema is semisolid, cool and nontender. Measurements at one time were as follows: right ankle, 35 inches (88.9 cm.); right calf, 44 inches (111.76 cm.); left ankle, 34 inches (86.36 cm.); left calf, 46 inches (116.84 cm.). After rest in bed for four days, the right ankle measured 30 inches (76.21 cm.); the left ankle, 33 inches (83.82 cm.); the right calf, 40 inches (101.6 cm.), and the left calf, 45 inches (114.3 cm.).

The basal metabolic rate ranged from —15 to —20 per cent. The Wassermann test was negative. Chemical examination of the blood showed 11 mg. of urea nitrogen, 65 mg. of sugar, and 427 mg. of chlorides, per hundred cubic centimeters. The dextrose tolerance test and urinalysis gave negative results. The blood count showed 5,240,000 erythrocytes, 7,600 leukocytes and 75 per cent hemoglobin. The results of the differential count were as follows: polymorphonuclears, 67 per cent; lymphocytes, 30 per cent; large mononuclears, 2 per cent; eosinophils, 1 per cent. Cultures of the blood gave negative results on several occasions. Cultures of tissue by Dr. McGuire showed hemolytic streptococci.

The mucous membrane is clear.

The febrile episodes continue to appear at somewhat less frequent intervals.

Treatment has consisted of administration of streptococcus vaccine and, later, of administration of antiserum (Foshay).

DISCUSSION

DR. LESTER HOLLANDER, Pittsburgh: The interesting thing is the dystrophia adiposogenitalis which the boy presents. The genitals are very small. I have observed a case of Milroy's disease in a boy aged about 10 years, in which a similar syndrome occurred. I do not know whether one is justified in calling the disorder a Fröhlich syndrome, but think that abnormality is of importance in conjunction with the other findings.

DR. R. A. C. WOLLENBERG, Detroit: As I understand Milroy's disease, it is quite distinct from the condition exhibited by this patient. I consider his disorder to be sporadic elephantiasis due to obstruction of the lymph vessels, with hypertrophy and edema, resulting from infection about the feet and toe-nails. Whether this condition is a fungous infection or one due to pyogenic organisms, it is quite distinct from Milroy's disease. In cases of the latter condition there is enlargement or hypertrophy of the legs without blocking of the lymphatics. It is a chronic hereditary disease and is probably of a trophic nature.

In this case focal infection could probably be eliminated by removal of the toe-nails.

DR. LEON GOLDMAN, Cincinnati: This patient had elephantiasis, which appeared when he was about 12. Several years later the episodes of cellulitis began to develop. The condition occurs in his family. My colleagues and I have tried repeatedly to find some cause for the cellulitis and the lymphangitis. Cultures of tissue have been made under various conditions. The sections of skin have been examined repeatedly for organisms, but none has been found. We intend to give the patient some streptococcus vaccine. We have asked the surgeons repeatedly to remove the toe-nails, but they think it inadvisable to do so before the infections subside for an appreciable length of time.

DR. FRED WISE, New York: I am curious to know whether there is any abnormality of the testicles, or anything suggesting Fröhlich's syndrome. I think this is an important point in the diagnosis.

DR. MARION B. SULZBERGER, New York: I agree with Dr. Wollenberg, and I wish to state that Dr. Williams and Dr. Traub in New York have recently investigated cases of recurrent erysipelas-like lesions of the legs and feet. I had an opportunity to see one patient and to study the disorder. That patient was tested with trichophytin applied by the usual method on the arm and intracutaneously. The reaction was negative after twenty-four and forty-eight hours. However, on the skin of the affected leg, proximal to the affected area, there was a strongly positive immediate reaction in the form of a wheal. There was also a high titer of passive transference antibodies to trichophytin in that patient's serum. Dr. Williams, Dr. Traub and I regarded that disorder as being due to a localized lymphatic or vascular immediate wheal type of sensitivity to fungi, and not erysipelas.

DR. LESTER HOLLANDER, Pittsburgh: I have studied a case of a similar disorder in which the same picture appeared on the dorsum of the foot.

DR. LEON GOLDMAN, Cincinnati: As to Fröhlich's syndrome, there is a typical clinical picture of that in this case, but all laboratory evidence is negative. He has received no treatment with pituitary extract. My co-workers and I still hold to the clinical diagnosis of Milroy's disease.

### LOCALIZED MYXEDEMA OF THE SKIN.

A. P., a Negress aged 32, has an irrelevant personal and family history.

Serologic tests and urinalysis gave negative results.

Biopsy revealed the typical picture of myxedema.

Little clinical change has resulted from the administration of thyroid extract, although the patient states that her legs felt better while she was receiving that medication.

Thyroid extract has been used as indicated; no local treatment has been employed.

#### DISCUSSION

DR. MAX SCHEER, New York: It seems curious that in a certain proportion of these cases the patient is likely to show hyperthyroidism rather than hypothyroidism. That may be one reason for the lack of therapeutic response to thyroid. What do the determinations of basal metabolic rate show?

DR. A. B. LOVEMAN, Louisville: Determinations of the basal metabolic rate were made and the rate was over normal before operation. After operation it

has varied somewhat. My colleagues and I decided to present this patient because we believed that she exhibits good examples of the three types of lesions that are described in cases of circumscribed myxedema, namely, the diffuse thickening of the skin, the localized nodular thickenings and the keloid-like papules. We were not certain whether the lesions were keloids, therefore an additional biopsy was made, which revealed myxedema.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: This plaque shows the typical features of so-called circumscribed myxedema. Occurring, as is usually the case, in association with hyperthyroidism, it represents an unusual physiologic paradox. The lesions occur on the lower portion of the legs, almost without exception; this may possibly be explained on the basis of circulatory stasis gradually interfering with the supply of thyroid hormone to these parts.

KRAUROSIS VULVAE.

B. T., a woman aged 51, has complained of some pruritus of the genitalia for the past five years, but recently the condition has become considerably aggravated. No therapy, except local applications of various ointments and lotions, has been used. The patient has received treatment for latent syphilis for the past two years. No details were available concerning her syphilitic infection. A panhysterectomy was performed in 1915.

There is no family history of syphilis, tuberculosis or malignant disease. Some mental insufficiency is noticeable, but otherwise there are no abnormalities. No leukoplakia buccalis is present. There is almost complete obliteration of the labia pudendi. The skin is thickened. Vaginal inspection shows no abnormalities.

The Kahn test was positive. Urinalysis gave negative results until recently, when inconstant glycosuria was found for the first time. A dextrose tolerance test showed diminished tolerance.

Histologic examination of a section showed atrophy of the epithelium; few papillae were seen; rare areas of the epidermis, at one edge of the section, showed vacuolation and some irregular grouping of prickle cells; few mitoses were also present in these areas; there was lymphocytic infiltration in the derma; some increase in fibrous tissue and a few glandular appendages were also observed.

Treatment has consisted of local application of soothing preparations and of injections of pituitary extract and ovarian extract. The diabetes is controlled at present with dietary restrictions.

DISCUSSION

DR. LESTER HOLLANDER, Pittsburgh: The treatment of kraurosis vulvae should consist of complete and radical vulvectomy, and this should be done early. Dermatologists should not temporize with roentgen therapy or other forms of treatment because delay may be serious as these lesions are potentially malignant.

DR. EARL D. OSBORNE, Buffalo: I agree with Dr. Hollander regarding vulvectomy in cases of true kraurosis vulvae. I believe, however, that section of the pubic and long pudendal nerves is also essential for permanent results. I believe that it is the practice at the Mayo Clinic to sever those nerves. My colleagues and I have had three patients who were treated in that manner, and splendid results were obtained.

DR. MARION B. SULZBERGER, New York: I was interested in this case particularly because of the lack of leukoplakia. It is a case of kraurosis associated with latent syphilis but without leukoplakia.

I wonder whether any of the members have had any experience with theelin therapy in cases of pruritus vulvae. It is known that this hormone has a marked effect on the vulvar epithelium, demonstrable in infants and young children. It increases the cornification. I have treated one patient with intractable pruritus vulvae with injections of theelin and have obtained apparently excellent results. The pruritus stopped, after many years' duration, and without other therapy.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: This type of true kraurosis vulvae, with or without leukoplakia, should be distinguished from the more com-

mon neurodermatitis of the vulva with lichenification in cases of which subjective symptoms of pruritus are more prominent. Because of the prospect of ultimate malignant degeneration in this case the treatment of choice is surgical resection of the vulva. Whether the pudendal nerves should be resected is dependent on the degree of symptomatic discomfort that exists in any given case.

Dr. Frank W. Cregor, Indianapolis: I wonder what effort has been made to demonstrate a fungus in this case. In my opinion the disorder lacks many of the features of kraurosis.

I had the nurse remove the patient's slippers and I found a mycotic infection between the toes of both feet. I think that careful examination should be made before subjecting the patient to a vulvectomy.

Dr. H. L. Claassen, Cincinnati: My co-workers and I have found no evidence of any fungous infection.

Squamous Cell Carcinoma of the Right Foot with Inguinal Metastases.

Mr. E. K., aged 62, says that this condition began in 1932 with a "callus" on the sole of the right foot. He operated a power machine and believed that this "callus" followed continued operation with the right foot. In January 1934 he first complained of soreness, and at that time the "callus" seemed to become rougher and larger. He consulted a physician, who gave him some form of chemical cauterization and special shoes, but this produced no relief. The lesion continued to grow and became more painful. He was admitted to the hospital in January 1935. There is no family history of malignant disease of any sort.

Photographs showing the progress of the lesion from a large fungating papillomatous mass to the present ulcer are presented. Firm glands in the right inguinal area were noted only four months ago.

The Kahn reaction and urinalysis were negative. Roentgenograms of the metatarsus gave negative results. There was some rarefaction in the distal phalanx of the right big toe.

Biopsies have been made at intervals and showed early development of squamous cell carcinoma. Biopsy of material from the inguinal gland also showed squamous cell carcinoma.

In the early part of March 1935 complete electro-excision and electrocoagulation were employed. These procedures were followed shortly afterward by roentgen therapy, a total of 2,712 roentgens of unfiltered radiation being administered. The patient is receiving roentgen radiation to the inguinal glands.

DISCUSSION

Dr. I. J. Arnsson, Buffalo: I suggest a diagnosis of ulcer following surgical removal of a benign papilloma. All the slides presented failed to show malignant degeneration, and the so-called metastases in the lymph gland failed to show any squamous cells. The so-called islands of epithelial cells were surrounded with basal cells.

Dr. Elmore B. Tauber, Cincinnati: This patient originally exhibited what I thought was papilloma of the foot; there was a great deal of secondary involvement. I insisted on that diagnosis, but gradually because of the great weight of opinion and of the biopsy report I reluctantly relinquished my diagnosis. I am glad that Dr. Arnsson brought out that point, for that was my original diagnosis.

Dr. H. Jerry Lavender, Cincinnati: At least half a dozen sections were sent to different pathologists in various places and the consensus was that the condition was squamous cell carcinoma.

Dr. A. B. Loveman, Louisville, Ky.: It should be emphasized that occasionally good general pathologists report the presence of carcinoma in material which undoubtedly exhibits examples of pseudo-epitheliomatous hyperplasia. This occurred recently on two occasions of which I am aware. One section was taken from the edge of an ulcer and the other from a hypertrophic growth on the vulva of a patient with lymphogranuloma inguinale.

DR. I. J. ARNSSON, Buffalo: I wish to call attention to an article which Weidman and White wrote some years ago on the technic of sectioning material for biopsies. If the sections are cut the wrong way one may get pictures which are similar to those of so-called malignant conditions. It is always advisable to examine the sections under high magnification. In true malignant degeneration such as squamous cell carcinoma one would not see islands with basal cells around them, but in the case under consideration one cannot demonstrate a single section without a border of basal cells.

DR. MAX SCHEER, New York: It is possible to mistake the excessive acanthosis of the margin of an ulcer for basal cell epithelioma. But in this case the inguinal gland showed squamous cell carcinoma.

EPIDERMOLYSIS BULLOSA.

This boy, aged 2 years, has an eruption which has been present since birth. There is no family history of any type of cutaneous disease. The mother and father are living and well.

Physical examination gave essentially negative results. The skin presents all the classic lesions of the disease.

The results of laboratory examination were negative.

Biopsy showed extensive separation of epithelial layers with formation of vesicles; there was some lymphocytic infiltration in the corium; no staining for elastic tissue was done.

Bullae continue to develop at points of trauma, especially on the hands and feet.

DISCUSSION

DR. RICHARD S. WEISS, St. Louis: I wish to ask whether the presenter made studies of the apparently normal skin for loss of elastic tissue. Many of the members may recall that Engman and Mook and also Kanoky and Sutton reported diminution and fragmentation of the elastic tissue of the apparently normal skin of patients with epidermolysis bullosa. I subsequently was able to confirm these observations.

DR. ELMORE B. TAUBER, Cincinnati: Such an examination was not made. The sections did show loss of elastic tissue, but no biopsy of the normal skin was made. The only thing I thought remarkable in this case was the response to the therapy used. The normal oil of the skin containing stearin was used, and in addition ultraviolet radiation, extract from the anterior lobe of the pituitary and small doses of thyroid extract were given. Originally by rubbing, a bulla could be produced at any time, but the members may have noticed that rubbing the patient's soles or body today did not produce the same response. The child is only 2 years old and, of course, one does not know what will happen.

DR. LESTER HOLLANDER, Pittsburgh: I do not wish to discourage Dr. Tauber about his treatment, which is excellent, but I wonder whether the same result would not have occurred without treatment. I think that these disorders improve as the patients grow older.

DR. WILLIAM H. GUY, Pittsburgh: My opinion is that epidermolysis bullosa has some connection with glandular disturbances. In many children the disorder clears up or improves at puberty. When the condition develops after puberty it does not respond to any therapy. Recently Beinhauer has tried treatment by injections of theelin and has reported clearing of the lesions. My co-workers and I have tried that method of treatment in two cases without effect. I believe that the administration of estrogenic hormone should be given a trial in the early phases of the disease.

EPIDERMOLYSIS BULLOSA, FORME FRUSTE.

Miss F. S., white, aged 20, has a congenital abnormality of the finger-nails and toe-nail, which has been present since birth. There were no cutaneous lesions until 1930, when painful blisters, large and small, began to appear spontaneously

over the feet. They seemed to respond slightly, but not entirely, to local application of various ointments. The skin in general is somewhat dry, and there is a mild acne of the face. There is no family history of a similar condition or of syphilis or tuberculosis.

General examination gave essentially negative results. The nail of the left large toe was removed surgically about three years ago; otherwise the nails show no changes. Spontaneous bullae appear on the normal skin chiefly at the base of the toes on the dorsa of the feet. The large oozing areas on the soles dry at times, heal with great difficulty and shortly afterward break down again.

Scrapings and culture were negative for fungi.

The patient has been under observation for a year and a half. The bullae which appeared spontaneously at the base of the toes have healed at times. The large areas on the feet seem to dry up considerably after roentgen therapy, but a relapse soon occurs.

The patient has received 1 erythema dose of roentgen radiation in divided doses. Local therapy has consisted chiefly of baths of potassium permanganate and application of calcium chlorate ointments.

DISCUSSION

Dr. S. S. Greenbaum, Philadelphia: In addition to the thickened nails, this patient has an oral abnormality. The lateral borders of the tongue show a thickened whitish condition which resembles leukoplakia. I think that the condition belongs in the group described by Jadassohn under the name pachyonychia congenita. A case somewhat similar to this one was described recently by Cole, Rauschkolb and Toomey.

Dr. Howard J. Parkhurst, Toledo, Ohio: Why was roentgen therapy used in this case?

Dr. Fred Wise, New York: I think the disorder presents most of the features of pachyonychia congenita described by Jadassohn, and I do not think that it is epidermolysis bullosa.

Dr. William H. Guy, Pittsburgh: I had great difficulty in agreeing with the diagnosis of epidermolysis bullosa, and I am pleased to hear Dr. Wise's remark. I wish he would elaborate on the changes in the skin which simulate epidermolysis bullosa and on the method of development. Does he believe that these cutaneous lesions have the same etiologic background as the changes in the nails?

Dr. Fred Wise, New York: In the few cases of pachyonychia congenita associated with dermatitis and hyperkeratotic lesions which I have seen there were also changes in the nails and on the tongue. I think there is an artefact in this patient. The patient was treated and removed the top layer of skin; this produced a lesion like one of epidermolysis bullosa. The spaces between the toes presented areas like eczema in the few cases of this condition which I have seen.

Dr. Isadore Rosen, New York: I wish to make one or two other suggestions in regard to this case. In view of the repeatedly negative results of examinations for fungi, I think one should consider the possibility of pustular psoriasis or acrodermatitis continua of Hallopeau.

Epidermolysis Bullosa (?).

This child, aged 2 years, has lesions which appeared at 3 months of age and consisted of vesicles and bullae distributed over the head, face, arms, legs, toes and fingers. When the patient was 1 year of age, severe ulcerative stomatitis associated with the cutaneous lesions developed. No similar disorders are known to have occurred in the family.

Bullae are present on the extremities, and there is atrophy at the site of former lesions.

Physical examination showed no essential findings other than malnutrition.

The Wassermann reaction was negative. Examination of the urine showed albumin (1 plus). The blood count showed 4,700,000 erythrocytes and 19,300 leukocytes; the hemoglobin content was 10.5 Gm. per hundred cubic centimeters. The results of the differential count were as follows: polymorphonuclears, 62 per cent; eosinophils, 6 per cent; lymphocytes, 25 per cent; large mononuclears and transitionals, 7 per cent. Tests with tuberculin gave negative results. Culture of material from bullae gave negative results on several occasions; then Streptococcus viridans and Oidium albicans were obtained.

Biopsy showed irregular separation of epithelial layers; no definite bullae were seen; there was scattered polymorphonuclear and lymphocytic infiltration in the corium, with some perivascular distribution; no staining for elastic tissue was done.

There has been improvement, especially of the lesions in the mouth.

Treatment has consisted of administration of viosterol, of a preparation of carotene and of brewers' yeast; local treatment with neoarsphenamine, and generalized treatment with sodium thiosulfate.

DISCUSSION

Dr. Toulmin Gaines, Mobile, Ala.: In these three cases there is no family history of consanguinity.

Dr. Lester Hollander, Pittsburgh, Pa.: I wish to call attention to the treatment in this case, namely, administration of viosterol, of a preparation of carotene and of brewers' yeast, local treatment with neoarsphenamine, and generalized treatment with sodium thiosulfate, as compared with the treatment in the previous case, in which excellent results were likewise obtained.

Dr. R. G. Senour, Cincinnati: I saw this patient at the Children's Hospital about three weeks ago, and all this therapy had been used before that time.

Dr. Richard S. Weiss, St. Louis: This patient's condition interests me because of the fact that my colleagues and I have a patient with a like disorder at the Children's Hospital in St. Louis. Because we could not come to any definite conclusion we diagnosed the condition as epidermolysis bullosa with a question mark, and the question mark is still there. In that case the lesions tended to disappear at certain seasons and recurred. Was a like variation noted in this case?

Dr. R. G. Senour, Cincinnati: According to the history there is no seasonal variation in this case.

Dr. Frank W. Cregor, Indianapolis: I believe that the reticulo-endothelial system supplies the means whereby the epidermis is held fast to the derma and that a defect in that system accounts for the development of the syndrome called epidermolysis bullosa hereditaria.

I believe that changes in the body structure which result from hormones coming into the circulation at puberty account for the improvement observed in cases of this disorder at that time.

Acute Lupus Erythematosus (Recovery).

L. V., a woman aged 26, was first seen on May 16, 1935; she had a cutaneous disorder of three weeks' duration, which began as small reddish blotches. There was no pruritus. The patient was sent to the hospital on May 27.

There are no physical abnormalities. When the patient was first seen she had six discrete maculopapular lesions on the side of the nose, face and forehead, which were slightly scaly and slightly burning; within nine days the lesions coalesced, forming a typical bat wing, slightly elevated lesion involving the nose and cheeks symmetrically. The temperature is 99.8 F. One erythematous lesion is present in the center of the hard palate. Lesions which appeared later are present on the extensor surfaces of the arms.

Examination of the blood on May 20 gave normal results. The urine was normal until serum sickness developed. Daily blood counts showed leukopenia.

Roentgen examination of the chest gave negative results. Culture of the blood gave negative results on two occasions while the patient was in the hospital; the sedimentation rate was decidedly increased.

No biopsy has been made.

The patient had a slight elevation of temperature and became progressively worse after admission to the hospital. The intensity of the eruption increased.

She was given 180 cc. of antistreptococcus serum (prepared by Foshay) intravenously, 60 cc. being given daily for three days. There followed severe and prolonged serum sickness, lasting fifteen days, with massive enlargement of lymph glands and marked and continuous urticaria associated with purpura and severe pains in the joints. The eruption began to fade after the second week, leaving some brownish pigmentation and slight scaliness. The patient left the hospital in three weeks, and the outline of the eruption could be plainly seen for two or three months.

DISCUSSION

DR. RICHARD S. WEISS, St. Louis: This case is labeled one of "acute lupus erythematosus (recovery)." I do not think that recovery has occurred. The patient presents a type of lupus which my co-workers and I have been recognizing for quite a while and to which Dr. M. F. Engman Sr. has called our attention on numerous occasions. In this type of condition there is a faint erythematous, slightly scaling eruption at first limited to the face and with only a suggestion of atrophy. It usually occurs in women aged between 17 and 30, especially in those who are under a severe social strain and who are living an active life. The cases of this disorder which we have observed have led us to believe that this particular type of lupus erythematosus is often the precursor of the acute exanthematic lupus erythematosus; I regard the prognosis in this case as grave, especially as the patient has leukopenia.

DR. DANIEL J. KINDEL, Cincinnati: In one way I am glad to hear Dr. Weiss say that this patient still has lupus erythematosus disseminatus, because there seems to be some question as to whether she has had that disease, and the residual markings can scarcely be detected. One must recognize that in the management and therapy of the acute disseminated form of lupus one is grasping at straws for a solution. In most cases the condition terminates fatally.

Three months before this patient was first seen, my co-workers and I treated a boy, aged 15, who after three weeks' hospitalization and a stormy course died of lupus erythematosus disseminatus. He was toxic, and the disease was far advanced when we first saw him. Culture of the blood on two occasions shortly after admission gave negative results. The boy did not receive the serum which we used in this case. He died as the result of an invasion by hemolytic streptococci, and autopsy showed all the cavities of the body filled with a brick-red fluid. I am aware of the fact that some observers consider septicemia in these cases as a secondary or terminal invasion. The organism was recovered and a vaccine prepared for possible subsequent use.

The woman who is presented also had a negative blood culture on admission to the hospital, but in view of our recent experience we decided to administer a specially prepared and potent antistreptococcus serum, prepared by Dr. Lee Foshay of the bacteriology department of the University of Cincinnati. The woman was tested with the vaccine for sensitization to the streptococcus recovered from the boy and showed a slight but positive reaction. One hundred and eighty cubic centimeters of serum was given intravenously within three days, 30 cc. of serum being injected morning and evening. Within a week there developed a severe serum sickness, lasting for fifteen days, with marked generalized lymphadenopathy involving even the nodes of the scalp. There were marked headache, arthritic pains, petechial hemorrhages in the skin and gastro-intestinal disturbances. Until shortly before the termination of the serum sickness the lesions on the face and arms persisted; later they faded gradually. When the patient left the hospital the lesions were still noticeable, but very faint. She continued to improve at home, and she

now has no lesions except residual patches consisting of slight atrophy and roughness of the affected areas with a scarcely discernible border. It is now five months since she was discharged from the hospital.

My colleagues and I considered this case worth presenting because of the therapy used, and we hoped that it might prompt others to use antistreptococcus serum in similar cases.

DR. S. W. BECKER, Chicago: I wish to call attention to the fact that vaccine or serum therapy must be used with great caution. My co-workers and I had one patient who had received vaccines. We treated her with quinine orally, but she became worse and died in a few weeks. In another case a surgeon had made a diagnosis of erysipelas and given antierysipelas vaccine, and the patient became acutely ill after receiving the treatment. Patients with this condition are highly sensitive to vaccine or serum of any kind, and it must be used with great caution.

DR. DANIEL J. KINDEL, Cincinnati: I cannot subscribe to the opinion that our treatment was too drastic, for this disease is so uniformly fatal that I do not see how much, if anything, is to be lost by proceeding with serum therapy properly controlled. In this case we had the advantage of consultation with Dr. Lee Foshay, an expert on serum therapy, who provided us with the material.

NOTE.—The patient is well at present and the skin is clear.

LUPUS ERYTHEMATOSUS.

Mr. F. R., aged 37, states that lesions appeared on his face in 1925, after he sustained a burn. There are no subjective symptoms and no known familial history of pulmonary, glandular or osseous tuberculosis, rheumatic fever, heart trouble or syphilis.

Physical examination gave negative results. On admission to the clinic in 1929 there were typical butterfly lesions over the face and along the sides of the neck. The hands were clear.

The results of the Wassermann test and urinalysis were repeatedly negative.

No biopsy was made.

This patient is presented chiefly because of the therapeutic aspect of the case. He received 5.5 Gm. of neoarsphenamine from June 28, 1929, to Jan. 30, 1930. From Oct. 11, 1929, to the present time he has received gold and sodium thiosulfate. The first few doses consisted of 0.1 Gm.; then 0.3 Gm. was given regularly. One hundred and eighteen injections were given, and the total amount of gold and sodium thiosulfate administered was 32.5 Gm. Periods of rest, averaging one month, were given every five to six months. No local or systemic reactions were noted. Considerable scarring remains.

DISCUSSION

DR. RICHARD S. WEISS, St. Louis: I was much impressed with the therapeutic result in this case, but when I read that 32.5 Gm. of gold and sodium thiosulfate was administered in a period of six years I was astonished. That seems to be a terrific amount. My co-workers and I are becoming more and more cautious the more treatment with gold compounds we use and the more we observe its effect on the leukocyte count. I wish to issue a warning that patients who receive gold preparations must be carefully watched; often excellent results can be obtained with a minimum amount of a gold preparation.

DR. ELMORE B. TAUBER, Cincinnati: When Dr. Wright read his paper last May I reported this case and stated that it was the exception which proved the rule.

DR. R. G. SENOUR, Cincinnati: I have treated this patient with a gold preparation for five years, and at the last meeting he had received 7.5 Gm. I was then warned. I watched him carefully. He has received 32.5 Gm. of gold and sodium thiosulfate all together. I think this patient shows real tolerance for the drug.

CHRONIC TULAREMIA (?) WITH AXILLARY ADENITIS.

Mrs. V. W., aged 42, in 1930 had an infection of the left hand after she dressed a rabbit. Shortly afterward there appeared enlargement of the glands in the axilla and neck, and recently the glands in the right axilla became enlarged. The glands in the left axilla have been draining since 1931. A cutaneous test gave a questionable positive reaction for tularemia, but there were no agglutinins nor opsonins for Bacterium tularense. Culture of material from a gland showed only staphylococci. For the past two years the patient has received staphylococcus vaccine therapy from Dr. Foshay. Recently she has received considerable roentgen radiation over the axillary glands. For the past fifteen years she has had a moderate diabetes, because of which insulin medication and dietary restrictions are necessary. At times she has had pyoderma and furunculosis. She claims that she had rickets and osteomalacia in early childhood. In 1924 tetanus developed after an automobile accident.

The patient has one child who is well except for "eye disease." Otherwise, the family history is irrelevant.

The skin shows pyodermic lesions with secondary excoriations. There are no local reactions to insulin. Matted glands and sinuses are present in the axillae.

Physical examination gave essentially negative results; there was no evidence of marked vascular sclerosis.

The Wassermann reaction was negative. The patient has had hyperglycemia at times. Cutaneous tests for tularemia and a tuberculin test gave negative results. The spinal fluid was normal.

Biopsy showed acute and chronic inflammatory changes. No specific granuloma and no organisms were seen in the sections.

There has been little improvement in the condition. The patient is receiving roentgen therapy. Complete excision of the glands has been recommended.

DISCUSSION

DR. MAX S. WIEN, Chicago: This patient is presented with a diagnosis of chronic tularemia with a question mark, and with the statement that there were no agglutinins nor opsonins for Bact. tularense. If this patient had tularemia she would have a positive reaction to a test for that disease. The axillary involvement presents a clinical picture almost identical with that exhibited by a patient whom I presented before the Chicago Dermatological Society (ARCH. DERMAT. & SYPH. **31**:150 [Jan.] 1935), who had a positive reaction to the Frei test and an associated genito-anorectal syndrome of lymphogranuloma inguinale.

I think that the possibility of the axillary lesions' being due to the virus of lymphogranuloma inguinale must be considered in this case and that a Frei test should be done.

DR. NORMAN TOBIAS, St. Louis: I suggest the diagnosis of sporotrichosis in this case, because of the resemblance of the disorder to that in a patient I am taking care of at present. Has the pus been examined for Sporotrichum?

DR. W. H. GOECKERMAN, Los Angeles: I suggest the diagnosis of acarophobia with secondary cutaneous lesions resulting from scratching. The patient told me that she had worms which she picked out of the skin.

DR. MARION B. SULZBERGER, New York: I agree with Dr. Goeckerman. The patient said that she found little white worms in all the lesions and that these lesions "worked" and itched until she picked the worms out. Furthermore, she has anesthesia of the larynx and a reduced corneal reflex. I think that the diagnosis of acarophobia is certain but that it does not quite account for the axillary lesions and that there may well be a second disorder. I think the facts that the examination gave negative results for Bact. tularense and that the serologic and cutaneous tests were negative practically excludes the possibility of tularemia.

DR. JOHN ERIC DALTON, Indianapolis: I agree with Dr. Wien that the possibility of lymphogranuloma inguinale should be considered and that a Frei test

should be made. This case emphasizes again the importance of watching for cutaneous manifestations associated with this venereal entity. It has been my experience and that of my co-workers in about two hundred and fifty cases of lymphogranuloma inguinale that in certain cases, aside from the glandular picture, there are outbreaks of purpura, erythema nodosum and generalized papulopustular lesions, which, in certain respects, simulated a papulonecrotic tuberculid.

DR. H. L. BAER, Pittsburgh: Apropos of tularemia, I think that the history in this case is confusing. Tularemia is one disease in the presence of which the cutaneous test and also the agglutination tests may remain positive for a period of almost twenty years. I think that the negative results of the tests would exclude the possibility of tularemia in this case.

DR. HOWARD HAILEY, Atlanta, Ga.: I agree with Dr. Sulzberger and Dr. Goeckerman that the condition of the skin is due to a pyogenic infection. The draining sinuses in the axilla, I believe, are likewise due to a pyogenic infection. Thorough curettage of the sinuses should bring about a speedy recovery. I have seen this clinical picture in the axilla several times previously. It usually occurs in patients with acne vulgaris, and this patient presents scattered lesions of acne.

DR. I. J. ARNSSON, Buffalo: I agree with Dr. Goeckerman and Dr. Sulzberger, and I suggest that autopyotherapy as demonstrated at the last meeting in Buffalo be used.

NOTE.—A Frei test was made and gave negative results.

ATOPIC ECZEMA; CONGENITAL SYPHILIS.

R. J., a Negro boy aged 3 years, was first admitted to the hospital on Feb. 15, 1935, and has been in the hospital since then. The condition appeared on the face five months before admission and then spread gradually to the scalp and extremities. The patient was born at full term, and delivery was normal. No details of the infant feeding are known. He had no illnesses of any sort before admission.

There is no known family history of allergy, tuberculosis or syphilis. Two other children in the family have no cutaneous diseases.

Physical examination gave negative results except for a persistent nasal discharge. No viscera were palpable in the abdomen.

On admission the patient had considerable oozing and edema of the entire face and scalp, associated with a generalized papular eruption.

The Kahn test was positive. Examination of the urine, a blood count and roentgen examination of the chest disclosed no abnormalities. Tests with human and bovine tuberculin and with all food and inhalant antigens gave negative results. Cultures suggestive of the Klebs-Löffler bacillus were obtained at times from the nose; virulence tests, however, gave negative results. Scrapings from the scalp showed no fungi.

Fever therapy was administered and the patient has since had no extensive oozing of the face. Papular eruptions still occur frequently. After a 100 per cent preparation of crude coal tar was applied a few months ago there developed increased swelling of the face, associated with drowsiness, oliguria and hematuria. No reactions followed application of 2 and 5 per cent coal tar ointments.

Treatment has consisted of elimination diets, including cod liver oil and calcium, courses of acetarsone, and administration of linseed oil. The Kettering hypertherm has been used; protective coverings have been applied to the patient's pillows and mattress. The patient has received local therapy to the nose, daily tar baths and local applications, chiefly of tar preparations.

DISCUSSION

DR. R. G. SENOUR, Cincinnati: I should like to have some therapeutic suggestions.

DR. MARION B. SULZBERGER, New York: I should like some suggestions as to the diagnosis. I can see no reason for calling this disorder atopic eczema. There

is no familial history of allergy, and that is one of the things on which the diagnosis of atopic dermatitis is based. The cutaneous tests have been negative, and that is a second point on which the diagnosis of atopic conditions is based. Furthermore, there was no demonstration of antibodies and none of eosinophilic cells. In my opinion this patient's condition should be classed in the vague group that is called "infantile eczema"; I am not able to tell whether it is the contact type or the seborrheic type; but it seems to me that the disorder is not an atopic dermatitis.

ATOPIC ECZEMA.

M. C., a girl aged 18, since early childhood has had cutaneous eruptions, characterized by periods of improvement and relapses, the eruptions occurring chiefly about the face, shoulders and upper extremities. In 1931, after the patient sustained an injury to the head, this eruption seemed to become much more severe and resistant to therapy. This injury also produced a partial detachment of the retina of the left eye. There are no symptoms associated with the cutaneous eruptions except "nervousness." For the past five years the patient has complained of episodes of typical hay fever occurring in the latter part of the summer and persisting until the end of September. The cutaneous condition is aggravated during these episodes. This summer (1935) she has had only slight attacks of sneezing; she was at that time receiving a course of treatment with the Kettering hypertherm. In 1933 the patient attempted suicide because of the severity of her cutaneous condition. She has frequently been hospitalized for observation. Tonsillectomy was performed in 1933.

There is no family history of any allergic reactions in the parents. A younger brother of the patient also has eczema. In one sister a cutaneous reaction results from wearing certain necklaces. One brother has no allergic history. There is no family history of syphilis or tuberculosis.

Physical examination gave negative results save for the detachment of the retina on the left.

The patient has been seen in all phases of the disorder, ranging from a generalized vesicular relapse with secondary impetiginization to a dry clear skin.

Studies of the blood gave negative results except for a persistent eosinophilia, the percentage of eosinophils ranging from 8 to 14 per cent. Urinalysis and roentgen examination of the skull gave negative results. In scratch tests with concentrated antigens positive reactions were obtained to the following foods and pollens: banana, rice, orange, cantaloup, tomato, celery, peach, grape, corn, orris, ragweed (strongly positive). Tests with the other common and uncommon food and pollen antigens were negative. Tests with the antigens which produced positive reactions were repeated after one year, and the reactions were all persistently positive. Patch tests with simple pollen and pollen oil of ragweed gave negative reactions. Patch tests with nickel and various cosmetic preparations likewise gave negative reactions.

No biopsy was made.

After a period of observation of about three years the following conclusions seemed justified: 1. Improvement of the cutaneous condition resulted simply from hospitalization, irrespective of local and systemic therapy. 2. Irritability in family life was considered an important factor in producing relapses. 3. Elimination diets plus application of coal tar ointment appeared to be the best practical temporary substitute for hospitalization. 4. Treatments with the hypertherm reduced the severity of hay fever this year, but they had no effect on the atopic eczema.

DISCUSSION

DR. R. G. SENOUR, Cincinnati: This is the type of disorder regarding which I, as a younger member of the dermatologic group, should like to obtain more information. Often these cases are passed over without discussion as to therapeutics.

DR. MARION B. SULZBERGER, New York: In this case I am inclined to agree with the diagnosis of atopic dermatitis. The question of therapy is difficult. As a

middle-aged member of the dermatologic group, I still find it difficult. The main difficulty is that as far as immunologic therapy is concerned the results in my experience are nil. As far as my co-workers and I have been able to carry out cutaneous tests and to check these by elimination and by renewed exposures to the substances eliciting positive cutaneous reactions, we have been unable to prove that many of those substances influenced the course of the dermatosis. After all investigations of this type we have to return to the old topical therapy. However, I must state that I, for one, have never been able to carry out the elimination and renewed exposure to my own satisfaction, for in all the cases of atopic eczema that I have studied the patients have given evidence of marked polyvalent sensitivity, and I have never been able to carry out elimination of inhalants simultaneously with elimination of foods and with other elimination tests. It is obvious that in these cases one cannot expect to get results by eliminating any one thing or any one group of substances. Hence, while there is no absolute proof that these disorders are due to hypersensitivity, one can say that the patients show hypersensitivity to cutaneous tests; and I believe that a perfection of methods for elimination of inhalants and foods may bring more satisfactory results. More encouraging is the fact that patients with atopic eczema often respond well to change of environment, and if possible they should have such a change. This points to a sensitivity to environmental factors. Unfortunately, it is often impossible to change the environment. Some of my patients have reacted well to a combination of therapy, and in the early attacks almost all have reacted well to roentgen therapy. In some cases we have checked (not cured) the disorder by giving repeatedly a mild dose of ultraviolet ray therapy, care being taken never to approach the erythema dose. In addition, we have obtained fairly good results with the ordinary stock "catarrhal" and other vaccines and with sedatives and preparations affecting the autonomic nervous system. But all in all, as a group there are many cases of atopic eczema in which the disorder is refractory to all known methods of therapy; and these present a distressing and as yet unsolvable therapeutic problem.

Dr. Fred Wise, New York: I suggest two therapeutic procedures with which I have had some success: The most important procedure is application of splints on the arms and legs; these are to be used regardless of the patient's objections. I have seen cases in which the use of splints alone cleared up 75 per cent of the lesions. Another measure is administration of a preparation of belladonna; this combined with phenobarbital has, I think, a better effect than any other drug or combination of measures.

Dr. Toulmin Gaines, Mobile, Ala.: I suggest that during recurrences the patient be given intravenous injections of strontium bromide.

Dr. S. S. Greenbaum, Philadelphia: I think that the members all agree that in cases of this sort there is more than one etiologic factor. The nervous element undoubtedly plays a large rôle, and whether this nervous influence is central or peripheral (autonomic nervous system) makes little difference. This element in this type of condition must be controlled in all respects if good results are to be obtained. Sedatives produce bad results in some cases; in others they are helpful. In one case I used strontium bromide intravenously four times daily for fifteen days and obtained a perfect result, which, I believe, was due to the fact that the vicious circle with the nervous instability as a link was destroyed.

Dr. T. W. Murrell, Richmond, Va.: Last fall I was a patient in a hospital, and I was rubbed with alcohol so frequently that there developed a dermatitis, which did not heal. Anything that was applied seemed to make the disorder worse, and finally I went down to Virginia Beach. It was in the winter, and I could not go into the surf, but I took salt water baths in the hotel, and that gave me complete relief. Any one can get some sea salt and use it in ordinary water, making a solution of about the strength of sea water. I have been impressed by the relief obtained. This is not a cure for allergic eczema, but it helps greatly in relieving the itching.

DR. LESTER HOLLANDER, Pittsburgh: I heard Dr. Sulzberger mention the use of ultraviolet radiation in cases of this disorder. Many of the patients exhibit involvement of the neck and arms and apparently have a photosensitivity, and I think that in view of that possibility it might be well to avoid the use of ultraviolet therapy.

DR. EARL EATON, Buffalo: Recently I had two patients with involvement around the face and neck, and small doses of ultraviolet radiation seemed to make the disorder worse. Three or four drops of solution of potassium arsenite three times a day appears to be helpful in some cases.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: My co-workers and I have recently observed six patients with this kind of neurodermatitis of atopic type in whom the tragic complication of ocular cataract has developed. One patient is aged 35; the other five are of adolescent age. In three there appeared to be a decided parallel relationship between the flare-ups of the cutaneous disorder and progressive loss of vision. The cataract, which is at first subcapsular, may proceed gradually to involve the entire substance of the lens; in two of the aforementioned patients there has been almost total loss of vision. If the usual exacerbations of the neurodermatitis are subdued or brought under control by careful management or possibly by change of environment, there may be no further progression of the cataract. Cataracts of this type can be detected in the incipient stage by careful ophthalmologic examination with the aid of the slit lamp, and it seems desirable to make such studies more generally in cases of neurodermatitis.

DR. WILLIAM H. GOECKERMAN, Los Angeles: So much has been heard about allergy in the last ten to fifteen years that whenever one sees such a disorder one wonders whether it is due to sensitization to protein. In one case in which the patient had been treated carefully but no result had been obtained I advised the patient to see a good internist. The patient was hospitalized, and the internist made careful studies of the blood and reported that he thought the patient's blood showed that he was not getting enough proteins, in spite of the fact that he seemed to be eating a well balanced diet. He was given a diet with an extremely high protein content. Within a few days his symptoms had practically disappeared. He remained in the hospital for a few weeks; the disorder cleared up completely and did not recur. Seemingly the entire result is due to the high protein diet. Whether this affects the nervous system or not I do not know.

### MYCOSIS FUNGOIDES.

N. P., a man aged 62, says that his cutaneous condition has been present for four years and that it has become worse during the last two years.

The patient's father died at 77 of pneumonia; his mother died at 68 of cerebral hemorrhage. Two brothers are living and well.

Erythematous, eczematoid and nodular infiltration is present over the entire body. An involvement representing an early stage of tumor is especially noticeable on the neck.

Physical examination showed generalized vascular sclerosis, chiefly arteriolar with hypertension, without congestive failure.

Serologic tests and urinalysis gave negative results. The results of the differential count were as follows: leukocytes, 11,200; polymorphonuclears, 68 per cent; lymphocytes, 18 per cent; eosinophils, 13 per cent; mononuclears, 1 per cent.

Biopsy showed extensive infiltration in the upper portion of the corium; this consisted of lymphocytes, eosinophils and so-called lymphoblasts. There also appeared to be considerable increase in the connective tissue.

The patient has received roentgen therapy and four intramuscular injections of chaulmoogra oil.

#### DISCUSSION

DR. ELMORE B. TAUBER, Cincinnati: This patient exhibits a rather classic picture. He had a premycotic stage of the disorder, but at present he has macules

and nodules on different sites. There are eruptions at some places, and on others there are flat scales. The condition has become progressively worse. About two months ago at the International Congress of Dermatology and Syphilology, which I attended, Dr. Lomholt reported two cases of mycosis fungoides in which chaulmoogra oil made by Bayer & Company had been used. Dr. O'Leary, who also was present, reported that he used the chaulmoogra oil prepared by Malinckrodt Chemical Company. This patient has complained of no pain at all. Dr. O'Leary said that his patients had some pain, but Dr. Lomholt said that there was no pain and that complete clearing occurred. It was a dramatic presentation. I cannot account for the results produced by the medicament, but I shall continue to use it.

### Lymphogranuloma Inguinale in a Child.

A Negro girl, aged 10, was admitted to the pediatric service of the Cincinnati General Hospital on March 16, 1935, because of a disorder which had appeared eight days previously. The history was obtained from the mother. One week before the onset of the acute symptoms the child complained of slight pain in both inguinal regions on walking, but no swelling was noted. Eight days before admission visible glands which were tender were noted; the glandular involvement became progressively worse. Fever was present from the onset of the acute symptoms but was not associated with chills. No vaginal discharge was noted by the mother, but repeated vaginal douches were ordered by a physician. No history of sexual indiscretion was obtained, and there was no history of onset of menstruation.

An uncle, living in the same house, stated that he had swelling of the inguinal glands in 1930. The mother had begun to take antisyphilitic treatment one year before.

On admission the patient was well developed and well nourished; the temperature was 102.4 F.; the patient appeared acutely ill. The skin was clear. There was no general lymphadenopathy except for palpable posterior cervical and axillary glands. The ears, eyes, nose and throat were normal except for slight injection of the pharynx. The heart, chest and abdomen were likewise normal. The liver and spleen were not palpable. No cuts or abrasions were noted on either extremity which might have accounted for the inguinal adenopathy. The inguinal glands bilaterally were markedly enlarged, measuring from 7 to 8 cm. in diameter. The tumor was hot, indurated and extremely tender. A moderate amount of redness was present. Vaginal examination gave practically negative results except for moderate injection of the mucosa. On rectal digital examination no glands were palpable and no stricture could be made out.

The blood count showed 4,300,000 erythrocytes, 8,500 leukocytes and 80 per cent hemoglobin. The results of the differential count were as follows: polymorphonuclear neutrophils, 71 per cent; lymphocytes, 28 per cent; monocytes, 1 per cent. A test with 0.1 mg. of old tuberculin gave negative results; the Kahn reaction was negative. Vaginal smears showed no pathogenic organisms on admission, but on April 4, 1935, one smear showed gram-negative diplococci. Roentgen examination of the chest gave negative results.

The results of cutaneous tests with Frei antigen were as follows:

| | Antigen | Reaction |
|---|---|---|
| Ten days after onset of acute symptoms | A | Questionable |
| Ten days after onset of acute symptoms | B | Negative |
| Ten days after onset of acute symptoms | C | Negative |
| Ten days after onset of acute symptoms | D | Negative |
| Fifteen days after onset of acute symptoms | E | Negative |
| Fifteen days after onset of acute symptoms | F | Negative |
| Twenty-three days after onset of acute symptoms | G | Negative |
| Twenty-three days after onset of acute symptoms | A | 3 plus |
| Twenty-three days after onset of acute symptoms | C | 1 plus |

The glands on both sides became fluctuant and required aspiration several times before vaccine therapy was started. Frei antigen was prepared from the

aspirated pus taken on the seventeenth day after the onset of acute symptoms and gave a strongly positive cutaneous reaction in four proved cases of the disease and a negative reaction in controls. Dark-field examination, smears and cultures of aspirated pus showed no pathogenic organisms. Cultures of tissue in Tyrode's medium were positive for the cultivation of a virus (Dr. Joseph Tamura). Heated cultured antigen gave a positive cutaneous reaction in seven proved cases.

Cutaneous tests with Frei antigen were made on members of the immediate family. The mother and a male roomer had strongly positive reactions; the father and the aunt had negative reactions.

Vaccine therapy with cultured antigen was started on the twenty-sixth day after the onset. The temperature, which had ranged between 101 and 102 F. since admission, had returned to normal. The glands at that time gave every indication of breaking down and again required aspiration two days after the administration of vaccine was started.

The vaccine was given subcutaneously on alternate days, a total of 10.25 cc. being administered in a course of twenty-two inoculations. The initial amount was 0.2 cc.; this was increased or decreased by 0.05 cc., depending on the previous local reaction. The maximum dose was 0.65 cc. No objectionable reactions were noted. Thirteen days later the child's condition had improved so much that she was discharged. The glands at this time showed only a small area of induration. The patient did not come to the clinic, and several months later both glands again broke down and drained. No rectal stricture has developed.

DISCUSSION

DR. SAMUEL GOLDBLATT, Cincinnati: This patient, I believe, is one of the youngest in whom the occurrence of lymphogranuloma inguinale has been reported. This disorder is peculiar in that it produces bilateral involvement of the inguinal lymph nodes in a female. This is an exceptional occurrence. The patient was treated with a specific type of serum and apparently made a good recovery, but a relapse occurred, and the child was then treated by partial excision and electrocoagulation of the involved glands.

LYMPHOGRANULOMA INGUINALE. LATE STAGE OF LATENT SYPHILIS.

R. F., a Negress aged 25, was treated for lymphogranuloma inguinale with sodium antimony biscatechol-di-sulfonate at the Cincinnati General Hospital five months ago. She again has a swollen labium, and there is no history of exposure. The condition started as a split in the labium, but this has now healed. The menses are regular. The patient had lymphogranuloma inguinale five years ago; this cleared up while she was at the workhouse. She has had three miscarriages. There is no history of gonorrhea.

The right labium minus pudendi is the seat of a granulomatous eruption extending about 5 cm. into the vagina and 3 cm. in length. On the surface apposing this labium minus on the right, the ulceration extends into the fold and up on the labium majus for an area of about 5 cm. The patient has lost 7½ pounds (3.4 Kg.) in the last few weeks, has felt weak and nervous and has complained of slight stinging on urination.

DISCUSSION

DR. SAMUEL GOLDBLATT, Cincinnati: The patient is presented because of therapeutic results. She was treated by deep coagulation of the entire lesion, and there has been no recurrence during a fairly long period. For several years she had been treated with antimony and potassium tartrate and with sodium antimony biscatechol-di-sulfonate, but there were constant recurrences. Electrocoagulation has been used by my colleagues and me for several years, and we have not seen a recurrence after its use.

DR. JOHN E. RAUSCHKOLB, Cleveland: Antimony therapy causes lymphogranuloma inguinale to heal with a thick keloidal scar, which when this therapy

is discontinued almost invariably breaks down, the process again becoming active. This reactivation can be explained by the fact that in this scarring Donovan bodies have been found. I believe that the best combination of methods in cases of this disease consists in using antimony therapy until scarring takes place and then removing the scar with electrocoagulation and treating the whole area intensively with roentgen radiation.

LYMPHOGRANULOMA INGUINALE. LATE STAGE OF SYPHILIS.

W. C., a Negro aged 29, states that about eight months ago there developed a "sore on his penis," which kept ulcerating and eroding away until at present the penis is almost all gone. He was treated at a clinic and was using some "stuff" himself. He was operated on at the workhouse. He states that he had gonorrhea once but has had no chancre and no hair cut.

There is no history of tuberculosis or cancer in his family.

There is a scar over the left labia pudendi. Examination of the mouth shows caries and pyorrhea. In the right groin there are two scars, each about 1 by 2 cm. There is bilateral inguinal adenopathy. The penis is missing. There are ulceration and erosion of the base, which is about 0.5 cm. long; it is covered with green, foul-smelling exudate mixed with red granulating tissue.

In January 1929 and in August 1935 the Wassermann reaction was 4 plus. On Oct. 23, 1935, the blood count showed 5,550,000 erythrocytes and 6,500 leukocytes.

No biopsies were made.

The patient has received ten injections of neoarsphenamine, a total of 5 Gm.

DISCUSSION

DR. SAMUEL GOLDBLATT, Cincinnati: This patient was treated with electrocoagulation, and healing resulted in six weeks. At present little can be seen of the previous lesions.

HEMANGIOLYMPHANGIOMA WITH ELEPHANTIASIS.

N. C., a girl aged 20 months, is presented from the orthopedic service of the Cincinnati General Hospital. The deformity has been present since birth. The child was born normally at term; she started to walk at 13 months and to talk at 18 months. There has been no sickness. There is no familial history of any similar conditions. Three other children are living and well. The mother had edema of the left leg at the time of the birth of the patient. Examination gave negative results except for changes in the cutaneous and subcutaneous tissues.

The skin is bluish; there are doughy swellings on the right side of the body, extending from the trunk through the right labium majus pudendi and the entire right lower extremity. The right foot and leg are considerably larger than the left. Nevi are present over both thenar eminences.

The Kahn test was negative. Roentgenograms of the right leg and foot and the lower portion of the spine and the pelvis showed no changes in the bones.

Several plastic operations on the right foot have been performed by Dr. Freiberg.

Biopsies showed areas of hemangioma with some increase in fibrous tissue; some areas showed angioma resembling lymphangioma.

DISCUSSION

DR. M. J. REUTER, Milwaukee: I thought of the possibility of an arteriovenous fistula.

DR. LEON GOLDMAN, Cincinnati: My co-workers and I have examined the child carefully, but we can find no evidence of an arteriovenous fistula. The

microscopic sections are interesting in that they show, in addition to areas of typical hemangioma, some areas of lymphangioma.

A Case for Diagnosis.

L. V., a woman aged 50, has had swelling of the genitalia for a few months. Examination revealed scars of an old small papulo-ulcerative eruption which was diagnosed in 1929 as syphilid, although the Wassermann reaction at that time was negative. The elephantiasis was noted at that time but was not as great as at present and did not contain any sinuses. Examination on July 6, 1935, revealed elephantiasis of the labia majora pudendi extending over the right buttock. The lesion over the buttock was perforated by many sinuses which contained purulent discharge.

General examination gave negative results except for irregular, slightly unequal pupils.

The Frei test gave negative reactions on two occasions, with four antigens. Tests with human and bovine tuberculin were negative on two occasions. The Wassermann reaction was consistently negative.

The patient does not know exactly how long the condition existed before 1929, when it was first observed by me. No attempt at therapy has been made.

DISCUSSION

Dr. G. S. Williamson, Ottawa, Canada: I suggest the diagnosis of lymphogranuloma inguinale with negative anergy. This is the type of condition which one might expect to be associated with negative reactions, just as in cases of extensive tuberculosis there are negative reactions to tuberculin. This is probably due to the fact that the power to form immunologic bodies has been lost.

Dr. Max S. Wien, Chicago: This case is a clinical example of the type of elephantiasis of the vulva seen in cases of lymphogranuloma inguinale, and there is, in addition, a dissecting cellulitis of the buttocks with purulent sinuses that resembles the picture in a case reported by Perlstein and me (Lymphogranuloma Inguinale, *M. Rec.* **139**:288 [March 21] 1934). In our case, Frei tests made in the usual manner were also negative. A positive Frei reaction, however, was obtained by cross-testing as suggested by Wise and Sulzberger (*J. A. M. A.* **99**:1407 [Oct. 22] 1932).

The presenter informs me that cross-testing has not been done. I believe that if this procedure is properly carried out in this case it will probably result in a positive reaction to the Frei test.

Dr. Marion B. Sulzberger, New York: There are undoubtedly certain cases which have been described in the literature by Wien and others, and in Europe as well, in which the condition was proved to be lymphogranuloma inguinale and in which there was a negative Frei reaction. I have observed two such cases. Whether or not one can describe these conditions on the basis of positive or negative anergy must be determined by finding out whether or not the patients have elaborated antibodies which will neutralize the Frei antigen. One must see whether the serum of such patients will neutralize the antigen, as was done in cases of sarcoid tuberculosis with tuberculin. This must be done in this case before one can speak of positive anergy.

Dr. Louis A. Brunsting, Rochester, Minn.: Examination of the right buttock reveals a large plaque of brawny induration with multiple sinuses which probably represents an extension of the process from the original site on the vulva. I should consider this to be pyoderma in a person with low resistance to the banal staphylococcus and with secondary lymphedema. Sometimes syphilis is a part of the picture, but antisyphilitic treatment alone will not bring about a cure. I suggest radical excision by cautery well beyond the most advanced border, followed after a suitable interval by plastic repair and grafts.

Dr. Arthur R. Woodburne, Grand Rapids, Mich.: I think one must consider in this case a combination of lesions which was recognized long before lymphogranuloma inguinale; it consists of perirectal abscesses and fistulas with secondary sinus tracts similar to these seen in this case over the buttocks and vulva. I wish to suggest this possibility.

Dr. Samuel Goldblatt, Cincinnati: I saw this patient for the first time six years ago, when she had a maculopapular eruption suggestive of syphilis. The Wassermann reaction was negative on several occasions at that time, and it has remained so ever since. At that time there was only a small involvement of the labia pudendi, that is to say, a slight swelling for which no cause could be found. The patient was not seen for the next five years, and when she was seen again, almost a year ago, the tremendous increase in size of the labia majora pudendi had developed. The Wassermann reaction is still negative. While the patient has undoubtedly had many opportunities for contracting syphilis as well as lymphogranuloma inguinale, I cannot believe that lymphogranuloma inguinale is present in this case in the face of the many negative Frei tests. It is certainly extremely rare to find an anergy both for syphilis and lymphogranuloma inguinale in the same patient extending over a period of years. Clinically, the patient had syphilis six years ago, and clinically she has lymphogranuloma inguinale now. However, the laboratory tests were negative six years ago and have remained negative.

# Book Reviews

**Nouvelle pratique dermatologique.** Volume I. Edited by Darier, Sabouraud, Gougerot, Milian, Pautrier, Ravaut, Sézary and Clément Simon. Price, 300 francs. Pp. 720, with 207 illustrations and 13 colored plates. Paris: Masson & Cie, 1936.

"Pratique Dermatologique," prepared under the editorship of Besnier, Brocq and Jacquet, has been, since its publication in 1900, a monumental and standard reference work of dermatology. It is now out of date and "Nouvelle pratique dermatologique" is designed to replace it. The new system consists of eight volumes containing a total of 7,350 pages, with 2,425 illustrations and 2,156 plates in color, and has been prepared under the direction of the eight dermatologists named, with the assistance of seventy-nine other representative members of the French school of dermatology.

The first volume, which treats of general dermatologic pathology, consists of ten sections. This volume was prepared under the direction of Darier by three of his former pupils and assistants, Civatte, Flandin and Tzanck, each of whom is more or less individually responsible for certain sections of the text.

The first section considers the difficulties of classification of dermatoses and contains an interesting review of all the important classifications from that of Willan in 1798 to that of Jadassohn.

The section on the anatomy of the skin comprises 92 pages, and its completeness is notable, while numerous illustrations and 6 excellent color plates add greatly to its value.

The physiology of the skin is fully considered in a section of 90 pages. The importance of its biochemical activity has received due recognition, and there are articles of varying length dealing, among other subjects, with the rôle of cevitamic acid, glutathione, cholesterol and the ferments of the skin, all of which furnish an excellent résumé of the latest knowledge of the activity of such agents.

An extensive section dealing with the general features of cutaneous histopathology, which also contains a wealth of excellent illustrations and a number of striking plates in color, constitutes a complete reference book on this subject.

The next two sections deal with etiology and pathogenesis, a particularly interesting portion being the division presenting an analytic study of the pathogenic mechanisms underlying diseases of the skin. Tables such as one showing the differential characteristics of the reaction due to intoxication and that due to intolerance and another giving a synoptic classification of diseases of the skin may be cited as illustrative of the valuable tables and charts found in the several succeeding sections.

The last section is a brief but adequate consideration of the general therapeutic principles of dermatology.

The format of the book deserves comment. The printing, illustrations and binding are extraordinarily fine and beautiful. Altogether, the volumes in this system are the handsomest the reviewer has seen in a medical book, and he has rarely seen handsomer volumes in any other type of books. The work is evidently intended to be a worthy successor to the earlier volumes, and it fully reaches that standard.

# Books Received

Di sensibele chronaxie. Lambertus Jan Hut. Groningen: M. de Waal, 1936.

# Directory of Dermatologic Societies *

## INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY
American Secretary: Dr. Howard Fox, 140 E. 54th St., New York.

## FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY
(CANADIAN BRANCH)

H. A. Dixon, President, Medical Arts Bldg., Toronto, Ont.
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg., Toronto, Ont.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

H. W. Barber, President, 7, Devonshire Pl., London, W. 1.
Louis Forman, Secretary, 7, Devonshire Pl., London, W. 1.

## NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Paul A. O'Leary, Chairman, 102 Second Ave., S.W., Rochester, Minn.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: Atlantic City, N. J.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.

AMERICAN DERMATOLOGICAL ASSOCIATION

C. Guy Lane, President, 416 Marlborough St., Boston.
F. D. Weidman, Secretary, University of Penssalvania, Philadelphia.
Place: New Ocean House, Swampscott, Mass. Time: June 4-6, 1936.

## SECTIONAL DERMATOLOGIC SOCIETIES

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cleveland. Time: Dec. 5, 1936.

MISSISSIPPI VALLEY DERMATOLOGICAL SOCIETY

Samuel Goldblatt, President, 3208 Colerain Ave., Ciscinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

Henry J. F. Wallhauser, President, Medical Tower, Newark.
Louis J. B. LeBel, Secretary, 165 Grant Ave., Nutley.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of January, March, May, September and November.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Jack W. Jones, Chairman, 384 Peachtree St., Atlanta, Ga.
Winston U. Rutledge, Secretary, 332 W. Broadway, Louisville, Ky.
Place: Baltimore. Time: Nov. 17-20, 1936.

## STATE DERMATOLOGIC SOCIETIES

CALIFORNIA MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, DERMATOLOGY AND SYPHILOLOGY SECTION

Thomas J. Clark, Chairman, 400, 29th St., Oakland.
George V. Kulchar, Secretary, 450 Sutter St., San Francisco.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY

Maurice J. Strauss, Chairman, 41 Trumbull St., New Haven, Conn.
Edward A. Abbey, Secretary, 442 Temple St., New York.

FLORIDA SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

J. L. Kirby-Smith, Chairman, 204 Laura St., Jacksonville.
W. M. Sams, Secretary, 310 Ingram Bldg., Miami.

LOUISIANA DERMATOLOGICAL SOCIETY

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harvey P. Towle, President, 453 Marlborough St., Boston.
Rudolf Jacoby, Secretary, 270 Commonwealth Ave., Boston.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Louis Tullipan, Chairman, 224 E. 17th St., New York.
C. H. Peachey, Secretary, 197 S. Goodman St., Rochester.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA SECTION ON DERMATOLOGY

Abraham Strauss, Chairman, Medical Arts Bldg., Philadelphia.
L. G. Bembauer, Secretary, 5026 Jenkins Arcade Bldg., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

A. E. Schiller, Chairman, 10 Peterboro St., Detroit.
G. Warren Hyde, Secretary, 2501 W. Grand Blvd., Detroit.

MINNESOTA DERMATOLOGICAL SOCIETY

L. H. Winer, President, 78 S. Ninth St., Minneapolis.
F. W. Lynch, Secretary, Lowry Medical Arts Bldg., St. Paul.
Time: First Wednesday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Charles P. Bondurant, President, 412 Medical Arts Bldg., Oklahoma City.
Darrell G. Duncan, Secretary, 914 Medical Arts Bldg., Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

J. C. Michael, President, 1215 Walker Ave., Houston.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Austin.

## LOCAL DERMATOLOGIC SOCIETIES

### Baltimore-Washington Dermatological Society

Dudley C. Smith, President, University of Virginia Hospital, Charlottesville, Va.
Francis A. Ellis, Secretary, 104 W. Madison St., Baltimore.

### Bronx Dermatological Society

Paul Gross, Chairman, 35 E. 84th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

### Brooklyn Dermatological Society

Samuel Hecht, President, 679 Greene Ave., Brooklyn.
Mortimer J. Cantor, Secretary, 907 St. Marks Ave., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

### Buffalo-Rochester Dermatological Society

Earl L. Eaton, President, 40 North St., Buffalo.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

### Central New York Dermatological Society

George M. Fisher, President, 264 Genesee St., Utica.
Rudolph Ruedemann Jr., Secretary-Treasurer, 214 State St., Albany.

### Chicago Dermatological Society

Max S. Wien, President, 104 S. Michigan Ave., Chicago.
Reuben Nomland, Secretary, 25 E. Washington St., Chicago.

### Cincinnati Dermatological Society

Raymond G. Senour, President, Carew Tower, Cincinnati.
Leon Goldman, Secretary-Treasurer, Doctors Bldg., Cincinnati.

### Cleveland Dermatological Society

H. G. Miskjian, President, 856 Rose Bldg., Cleveland.
E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

### Detroit Dermatological Society

W. G. Wander, President, 509 Kresge Bldg., Detroit.
G. Warren Hyde, Secretary-Treasurer, 2501 W. Grand Blvd., Detroit.

### Los Angeles Dermatological Society

N. P. Anderson, Chairman, 2007 Wilshire Blvd., Los Angeles.
Thomas W. Nisbet, Secretary, 65 N. Madison Ave., Pasadena, Calif.
Time: Second Tuesday of each month, October to May, inclusive.

### Manhattan Dermatologic Society

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

### Montreal Dermatological Society

B. Usher, President, 1538 Sherbrooke St., W., Montreal, Canada.
Paul Poirier, Secretary, 456 Sherbrook St., E., Montreal, Canada.

### New England Dermatological Society

William P. Boardman, President, 388 Marlborough St., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

Max Scheer, Chairman, 509 Madison Ave., New York.
Frank C. Combes, Secretary, 80 W. 40 St., New York.

NEW YORK DERMATOLOGICAL SOCIETY

R. H. Rulison, Chairman, 114 E. 62nd St., New York.
Eugene F. Traub, Secretary, 140 E. 54th St., New York.

OMAHA DERMATOLOGICAL SOCIETY

J. A. Borghoff, Chairman, 1319 Medical Arts Bldg., Omaha.
Donald J. Wilson, Secretary, 1113 Medical Arts Bldg., Omaha.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Vaughn C. Garner, Chairman, Germantown Professional Bldg., Philadelphia.
Thomas Butterworth, Secretary, 238 N. 5th St., Reading, Pa.

PITTSBURGH DERMATOLOGICAL SOCIETY

Emerson Gillespie, President, 120 Tuscarawas St., Canton, Ohio.
Joseph J. Hecht, Secretary, 506 Medical Arts Bldg., Pittsburgh.

ST. LOUIS DERMATOLOGICAL SOCIETY

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: Second Wednesday of each month.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

L. R. Taussig, President, 384 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.